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THE PATHOLOGY OF THE PARKINSONIAN SYNDROME FOLLOWING ENCEPHALITIS LETHARGICA, WITH A NOTE ON THE OCCURRENCE OF CALCIFICATION IN THIS DISEASE.

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CONTENTS.

I.—Historical Review.

II.—Account of Histological Findings in Two Cases.

III.—Relationship of Histological Changes to the Clinical Syndrome.

IV.—A Note on Calcification in Encephalitis Lethargica.

I.

Extremely few autopsy findings on cases of post-encephalitic paralysis agitans have been reported.

Marinesco [11] records the case of a man, aged 43, who had an acute attack of epidemic encephalitis in March, 1920, followed by paralysis agitans; he died in February, 1922. Although lesions were found in the globus pallidus they were much more intense in the locus niger. Here the cells for the most part had undergone cytolysis and their place was shown by masses of pigment. The neuroglial cells were increased in size and number in this region, and many of them contained pigment. The nerve fibres in the locus niger had largely disappeared. The vessels showed perivascular infiltration with small round cells; and the endothelium of the capillaries contained black pigment. The region of the red nucleus appeared practically normal.

McKinley [12] reports fully the histological findings in a man, aged 51, who died of paralysis agitans of two years' duration, following an acute attack of encephalitis lethargica. The globus pallidus, putamen and caudate nucleus showed insignificant changes as compared with those

found in the substantia nigra; they consisted of a moderate amount of chromatolysis and an occasional example of cytolysis, but there was no reduction in the number of cells. Slight perivascular infiltration was present in the globus pallidus but none in the putamen. In the thalamus the changes were rather more marked, but there was no evident reduction in the number of the thalamic neurones, nor was there any evidence of degeneration of nerve fibres in the basal ganglia. The lesions were most pronounced in the mesencephalon, especially in the substantia nigra; the cells were reduced to a small fraction of their normal number, and those remaining had without exception undergone chromatolysis. The pigment in the cells seemed to be increased, but this was attributed to shrinkage of the cells, which were smaller than those in a normal brain. The axis-cylinders were greatly decreased in number. A considerable amount of free pigment was scattered about and could be traced as far as the perivascular spaces. There was an increase of glia cells, and perivascular infiltration with round cells. Sections of the pons and medulla showed minimal changes.

Foix [5] reports a case in which the lesions were greatest in the substantia nigra, and consisted in atrophy of the cells with disintegration of the pigment, a process which proceeded in islets and finally resulted in cicatrization. In cases of idiopathic paralysis agitans which he has examined, the changes were most evident in the locus niger and globus pallidus, slightly predominating in the former.

Français and Lhermitte [6] report the autopsy findings in a male, aged 57, who had an attack of encephalitis lethargica in January, 1921; paralysis agitans followed in March, 1921. The patient committed suicide in September of the same year. Macroscopically depigmentation of the locus niger was noted. Microscopically the cells of the locus niger were much reduced in number and the remaining cells were distorted and depigmented. In certain parts there was no trace either of cells or of myelinated fibres. There was marked neuroglial overgrowth. The vessels of the locus niger showed perivascular infiltration with lymphocytes and plasma cells. The large motor cells of the corpus striatum were reduced in number and the remainder showed chromatolytic changes. There was considerable neuroglial overgrowth and perivascular infiltration. The small motor cells in the putamen and caudate nucleus were less affected. Lhermitte, in accordance with his pathological findings in cases of idiopathic paralysis agitans, concludes that the symptoms in this case were due to lesions in the pallidal system.

Mlle. G. Lévy [9] described the pathological changes in four cases

of paralysis agitans following encephalitis lethargica. She lays stress on perivascular disintegration in the basil ganglia, producing changes resembling *l'état criblé* and *precriblé* of Vogt. Precisely similar conditions to those depicted in her book were seen in my two cases and also in the normal brain which was used as a control, and they seem to be of the nature of artefacts. Degeneration of fibres in the ansa lenticularis and in the internal capsule, and changes in the corpus Luysii, red nucleus and fields of Forel were also present. The locus niger in every case showed depigmentation. The lesions in the mid-brain were subacute. There was degeneration in the antero-lateral columns of the cord. She concludes from the widespread nature of the process in her cases that no conclusions can be drawn as to the pathogeny of paralysis agitans.

Goldstein [8] describes a case in which the changes in the substantia nigra were the most prominent feature; his article is illustrated with excellent photomicrographs.

Trétiakoff and Bremer [14] report a case of a female, aged 47, who had an acute attack of encephalitis lethargica, of the ocular type, in December, 1919; this was rapidly followed by the Parkinsonian syndrome. A relapse occurred at the end of April, 1920, with fever, generalized pains, and incontinence of urine. She died on May 29, 1920, with hyperthermia. The inflammatory lesion consisted of an increase of lymphocytes, congestion of vessels and moderate neuroglial overgrowth. These changes were most marked in the mesencephalon, and particularly in the locus niger where the number of cells was considerably reduced. The remaining cells showed various degenerative changes. The cells of the red nucleus were normal. The authors were struck by the almost complete absence of inflammatory changes in the globus pallidus; they mention, however, the occurrence of calcification in certain of the large vessels in the globus pallidus. The putamen, caudate nucleus, and cerebellum were normal.

D'Antona and Vegni [2] describe the case of a male, aged 54, who had an acute attack of encephalitis lethargica in January, 1920, followed by the Parkinsonian syndrome. He died in February, 1921. The main incidence of the disease was found to have fallen on the substantia nigra, the cells being reduced to about a tenth of their normal number; inflammatory changes, though less marked, were also found elsewhere, as in the globus pallidus and nucleus dentatus. An excellent photomicrograph depicts the changes in the substantia nigra.

Vegni [16] reports a second case in a man, aged 20, who had an

attack of encephalitis lethargica, of the ocular type, in January, 1920, followed by paralysis agitans. He died in October, 1921, as a result of general peritonitis following an appendix abscess. The chief finding consisted in a great reduction in the number of cells of the substantia nigra with perivascular lymphocytosis. Degenerative changes were also found in the cells of the globus pallidus, dentate nucleus and locus cœruleus. He emphasizes the persistence of the infective process.

Gamna and Omodei-Zorni [7] report two cases. The first was that of a male, aged 29, who had an acute attack of encephalitis lethargica of the choreiform type, which was followed by the Parkinsonian syndrome. Histological examination showed an almost complete atrophy of the nerve cells of the substantia nigra and hypothalamus, associated with intense proliferation of neuroglial cells. Similar lesions, though slighter, were present in the globus pallidus, putamen, and caudate nucleus.

The second case was that of a woman, aged 27, in which the Parkinsonian syndrome did not become apparent for nearly two years after an acute attack of encephalitis lethargica. Lesions similar to those in the first case were found in the substantia nigra; the subthalamic region was very slightly altered and the corpus striatum was unaffected.

Urechia [15] reports the case of a male, aged 44, who for a year suffered from insomnia and periods of psychomotor excitement. There were no definite signs of organic disease in the central nervous system, except that his pupils were unequal and fixed. Although the Wassermann reaction was negative, he was given anti-specific treatment in view of the pupillary condition. Seven months later he presented definite signs of the Parkinsonian syndrome and a retrospective diagnosis of encephalitis lethargica was made. The patient died shortly afterwards. An autopsy showed intense inflammatory lesions in the basal ganglia, especially in the globus pallidus, corpus Luysii, and substantia nigra; less marked lesions were also present in the dentate nucleus.

II.

Histological Findings in Two Cases.

The following are the only two cases as yet in which I have had the opportunity of pathological study:—

Case 1.—A male, aged 41, came under observation in September, 1922, with well-marked paralysis agitans.

His wife stated that he had been quite well until an acute illness in May,

1921, characterized by double vision and marked sleeplessness. For more than a week he slept day and night and had great difficulty in swallowing. He was acutely ill for four weeks; it was then noticed that he was stiff and had considerable difficulty in moving. He improved, but was troubled with drowsiness for some months. The rigidity gradually became worse, so that feeding or dressing himself was impossible.

Examination in September, 1922, showed a very marked condition of paralysis agitans. It was impossible to understand his speech owing to the feeble voice; he was unable to dress and feed himself, and could scarcely move in bed; his head was slightly retroflexed, his mouth open, and he had marked sialorrhœa. His eyes had a staring expression. The pupils were regular in outline, equal and centrally placed; both reacted well to light and accommodation. The ocular movements were full and were carried out nearly as promptly as by a normal person, but there were a few initial nystagmoid movements in the extreme lateral positions; convergence was normal. The fundi were normal. Voluntary movements of the facial and jaw muscles were carried out feebly and slowly. There was slight weakness of the lower face on the right side which was apparent only on voluntary movement, as in showing the teeth. The tongue was protruded with difficulty, and was flabby and tremulous. The palate moved somewhat feebly on phonation. There was considerable difficulty in swallowing. The muscles of the neck were hypertonic, and there was loss of associated head and eye movements.

The posture of the arms was typical of paralysis agitans, especially that of the hands. The tone was considerably increased in all muscle groups, and the "cogwheel" phenomenon was well marked. All movements were carried out slowly and with difficulty. The reflexes were brisk and equal on the two sides.

At times there was a very slow rhythmical tremor of the true paralysis agitans type in both hands, the chief movement being one of alternating flexion and extension of the fingers. The rate of the tremor was four to the second. It was observed only when the limbs were at rest and never during voluntary movement. The musculature of the abdomen was hypertonic, the abdominal reflexes being excessively brisk. The posture of the legs was one of extension at the knees with the toes pointed downwards and the feet inverted; as in the arms there was moderate loss of power and tone was markedly increased in all muscle groups, but predominated in the post-tibial group of muscles and in the extensors of the knee.

The deep reflexes were brisk and equal; there was no ankle clonus; the right plantar reflex gave a doubtful extensor response, while the left was normal in type.

There was no disturbance of sensation in the arms, trunk or legs.

Progress.—The patient improved under hyoscine; his speech became clearer and he was able to turn more easily in bed.

On September 26 there was a rise in temperature with an accompanying increase in the respiration and pulse rate. The pyrexia became progressively

greater and on the day of his death—the 29th—the temperature was 104·6° F., respiration 60, and pulse 150. There was no clinical evidence of pulmonary implication.

An autopsy was performed ten hours after death. No abnormality was noted in the meninges. The brain and spinal cord were hardened in 10 per cent. formalin-saline for fourteen days.

A series of six horizontal sections was made through the basal ganglia, the thickness of each slab being approximately 4 mm. A portion of the tissue, including the basal ganglia, was taken from each slab and numbered; those from one-half of the brain being treated by the Weigert-Pal method, and those from the other by alum hæmatoxylin and van Gieson, and by Nissl's method. Photographs of each slab were taken for reference.

The mid-brain was cut in serial sections.

The brain from a man aged 40, who died as the result of an accident, was used as a control and was treated in precisely the same manner as the brain under consideration, the levels of the horizontal sections being approximately identical.

Histological Findings.

Cerebral cortex.—Beyond capillary dilatation there was no appreciable deviation from the normal. The cells were normal except for very occasional cytolysis. There was no diminution in the number of cells, nor was any perivascular infiltration observed.

Basal ganglia.—It may be said at the outset that no marked pathological changes were found in this region. The cells in the caudate nucleus and putamen were for the most part normal and were not appreciably diminished in number. Cytolysis was occasionally seen, especially in the putamen. Many of the cells stained poorly, were ballooned and had eccentric nuclei. Capillary dilatation was general. For the most part the vessel walls were normal, except for an occasional increase of cellular elements in them. Perivascular infiltration with round cells was not pronounced, but each section showed a few examples of this. There was no appreciable glial cell overgrowth.

Globus pallidus.—Many cells stained palely; chromatin granules were not apparent in the majority of the cells. This absence of chromophilic staining was noticed in all the cells of the basal ganglia and also in the control brain, and probably depended on faulty fixation. The vast majority of the cells were in every respect normal; rarely a cell with a markedly eccentric nucleus and an indefinite outline could be seen.

There was no diminution in the number of the large polygonal cells. The cells in ten consecutive fields were counted, and this was also done in sections from the corresponding blocks of the normal brain. Two different levels were taken, one from the middle of the lenticular nucleus and the other towards its caudal extremity. In each case the count from Case 1 exceeded that of the normal control.

The majority of the cells in the globus pallidus, and incidentally those

of the thalamus, showed a collection of pigmented granules which usually occupied half the cell. They stained green with toluidin blue. They were also present in the cells of the control though not to the same extent, and stained yellowish instead of green. In sections stained by Scharlach red they appeared as reddish granules in the cells, which points to the possibility of their being of the nature of lipochromes. Granules also could be seen scattered about in the surrounding tissue, and could be traced to perivascular lymphatic spaces. Similar appearances, though less marked, were also seen in the normal brain.

The vessels of the globus pallidus shared in the general vascular dilatation; occasionally perivascular infiltration by lymphocytes was observed, but this was only slightly more common than in the putamen and caudate nucleus. The walls in many instances showed an increase in the cellular elements.

In the sections stained by alum hæmatoxylin and van Gieson's counterstain, well-marked calcareous degeneration was observed in the walls of certain vessels. Such vessels were few in number, and were only seen in sections from about the middle of the basal ganglia. Further, the affected vessels were situated in the anterior portion of the globus pallidus and were evidently ascending vessels from the anterior perforated spot. In this region the arteries, veins and capillaries were all affected. In the majority of the vessels the deposit lay between the adventitia and the media. Hyaline degeneration was evident in the walls of those vessels that were only slightly affected; in some of these the deposit could be seen in the Virchow-Robin space. There was no thrombosis in any of the affected vessels. In the smaller vessels the cellular elements in the vessel walls were increased.

Thalamus. — The cells were not diminished in number. Cytolysis was relatively common, but the cells were for the most part otherwise healthy. Pigmentation granules were present in the majority of the cells. Perivascular infiltration was seen about as frequently as in the globus pallidus.

Sections from the lower three slabs showed acute changes in the subependymal region of the thalamus, and in that portion of the subthalamic region which adjoins the third ventricle. These changes consisted of numerous recent hæmorrhages in the perivascular spaces and surrounding tissue. Perivascular infiltration was here more marked than anywhere in the basal ganglia; similar acute changes were also noted in the infundibulum.

Corpus Luysii.—The cells appeared normal.

Sections stained by the method of Weigert-Pal showed no evidence of degeneration in the systems of fibres connected with the corpus striatum.

The mid-brain.—In this region the changes were distinctly more marked than in the basal ganglia, the greatest incidence of the disease having fallen on the substantia nigra. The pigmented cells were reduced to a small fraction of their normal number, and in their place were scattered particles of pigment which varied considerably in size. The few cells that remained showed various degenerative changes, such as eccentric nuclei, extrusion of the pigment, vacuolization and loss of the normal processes (fig. 2). Macro-

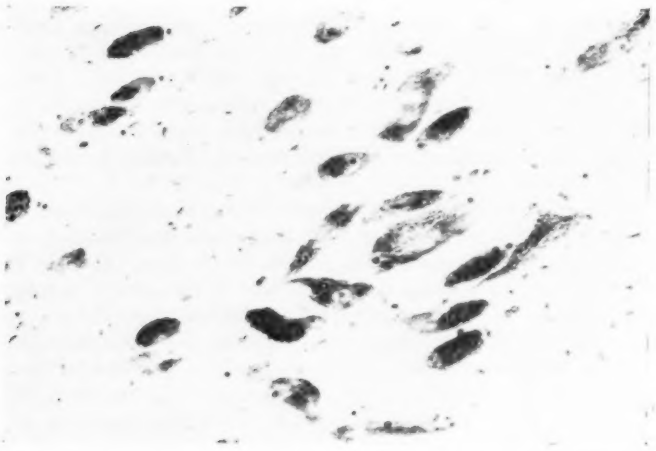

FIG. 1.—Photomicrograph × 300. Pigmented cells of normal substantia nigra.

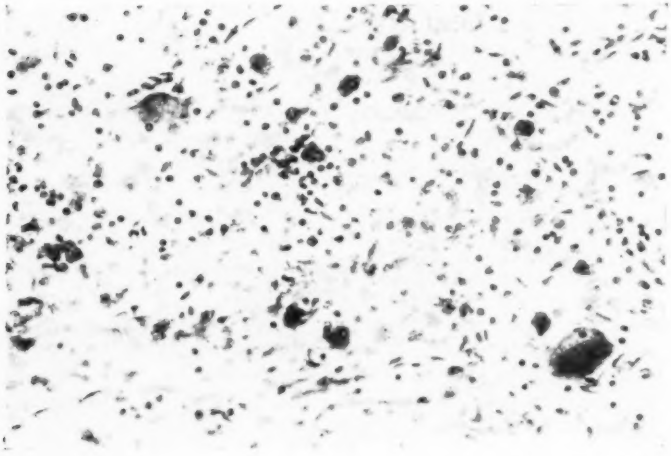

FIG. 2.—Photomicrograph × 300. *Case* 1. Parkinsonian syndrome of eighteen months duration. Substantia nigra showing marked reduction in the number of pigmented cells and scattered masses of free pigment. The two remaining cells in this field show cytolytic changes.

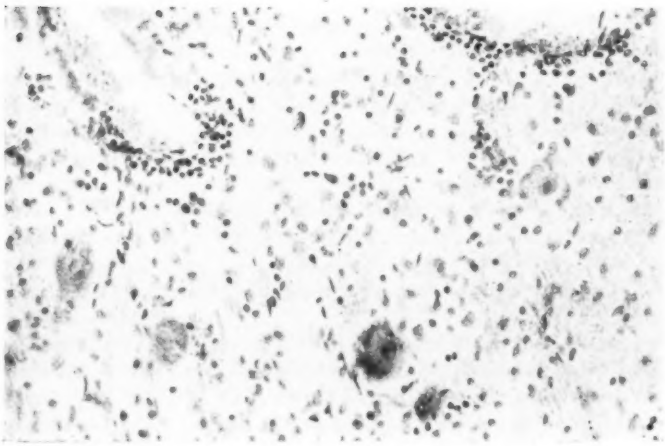

FIG. 3.—Photomicrograph × 300. *Case* 1. Perivascular lymphocytosis in region of substantia nigra, in addition to cytolytic changes in the cells.

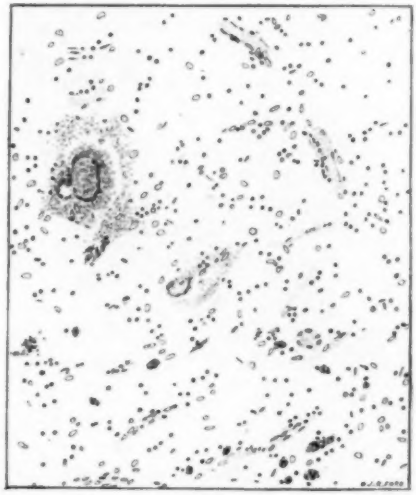

FIG. 4.—Camera lucida drawing × 100. *Case* 1. Recent perivascular hæmorrhages in region of substantia nigra.

and microphages of glial origin were plentiful, and many were packed with pigment. They could be traced to the perivascular spaces. In the walls of the larger meningeal veins in the interpeduncular space there were numerous particles of pigment; these also were evident in the lumen of the vessels, usually in the interior of the macrophages. Pigment was also present in these veins in the control brain, but it was in very much smaller amount than in this case. Perivascular infiltration was more prevalent in the mid-brain than in the basal ganglia (fig. 3). A few of the vessels showed hyaline degeneration of their walls.

Numerous recent hæmorrhages, similar to those described above as occurring in the thalamus, were present, especially in the ventral half of the mid-brain (fig. 4).

The glial cell overgrowth was not accompanied by a parallel increase in the glial fibres.

The cells of the *locus cæruleus* were not diminished in number; a few were depigmented and a small proportion of them showed chromolytic changes. The cells of the *third nucleus* appeared normal.

The smaller cells of the *red nucleus* were normal, except for fairly well-marked cytolysis. Some cells of the pars magno-cellularis showed definite changes, such as vacuolization, and several contained greenish granules of pigment; only a few of these cells appeared healthy. There was no apparent reduction, however, in their number.

Sections from the *pons* and *medulla* showed capillary dilatation and very moderate perivascular infiltration. No hæmorrhages were apparent. The cells of the nuclei of the lower cranial nerves were for the most part healthy, although in some there were chromolytic changes.

Sections from the cervical and dorsal regions of the cord were normal.

The Weigert-Pal method in sections from the pons and medulla showed no evidence of tract degeneration.

Case 2.—Female, aged 68, came under observation in February, 1923, with a condition of well-developed paralysis agitans.

She stated that she had been in good health until an attack of "influenza," about January, 1920. This illness was characterized by headache, pains all over, and marked sleeplessness. She also noticed that when she looked at anything close, as in reading, the letters ran together; she had never previously been troubled in this way. She gradually improved and at the end of a month was able to get up, but "she had never felt the same since." A few months later she noticed that she could not move her arms so quickly as formerly, and that she had a difficulty in getting upstairs. Somewhat later a tremor appeared in the left hand. In January, 1921, she suddenly lost the use of both legs. She remained in bed one month and the power of the legs gradually returned. In February, 1922, a similar attack occurred, from which she recovered fairly well.

On examination she showed a condition of moderate general rigidity with Parkinsonian facies. Her speech was slow and monotonous. The pupils were

unequal, the left being larger than the right; there was a definite right ptosis; this condition in the right eye was considered to be due to paresis of the right cervical sympathetic. The pupils reacted moderately well to light; but there was no reaction on accommodation. Convergence was much limited, otherwise the ocular movements were full.

The jaw and facial movements were feeble and slowly performed. There was slight weakness of the lower face on the left side.

The limbs on both sides showed the characteristic rigidity of paralysis agitans, but this was much more evident in the limbs on the left side. Power was considerably diminished and movements were performed slowly. There was tremor in both arms, rapid, coarse and exaggerated by movement.

The reflexes were more active on the left side, and ankle-clonus could be obtained on this side. The left plantar response was indefinite, whilst the right was probably flexor.

Examination of the heart showed evidence of left-sided enlargement; this was attributed to the general arteriosclerosis which was present. (Blood-pressure: systolic 240, diastolic 140 mm. Hg.)

A diagnosis of paralysis agitans, probably post-encephalitic, was made.

Course.—The patient improved on hyoscine, but on February 16 suddenly became acutely ill with dyspnœa and pyrexia; the temperature progressively rose and reached 104° F. on the third day when death occurred. Despite tachypnœa, no adequate signs to account for the symptoms could be found in the lungs. The cardiac condition showed no appreciable alteration from that present when she first came under observation.

An autopsy was performed six hours after death. Only the brain was removed. The membranes showed no gross abnormality.

The brain was hardened for ten days in formalin-saline and was then treated in a precisely similar manner to the brain of Case 1.

The following were the principal histological findings. All the cerebral arteries showed advanced arteriosclerosis.

Cerebral cortex.—Normal, no calcification of vessels.

Cerebellum.—Cells of Purkinje appeared healthy and the dentate nucleus was normal. No calcification or inflammatory changes were present.

Caudate nucleus.—Vessels shared in the general arteriosclerosis, the lumen of one or two of the arterioles was completely obliterated. Several of the vessels showed perivascular infiltration with round cells and capillary dilatation was general. The cells seemed normal except for pigment granules and occasional satellitosis.

Putamen.—A comparatively large hæmorrhage, not of recent origin, was seen in the anterior part of the putamen at its junction with the globus pallidus; the hæmorrhage partially involved the latter in its anterior part. Except in these areas the cells seemed normal. The vessels showed changes similar to those in the caudate nucleus.

Globus pallidus.—The anterior portion was partially involved in the

hæmorrhage mentioned above. Some of the vessels showed well-marked perivascular infiltration with round cells, but none of them were thrombosed. A few vessels in anterior half of the globus pallidus showed calcification of their walls. Except for the small area involved in the hæmorrhage the rest of the globus pallidus contained healthy motor cells, except for pigmentation and occasional satellitosis.

Internal capsule (right).—The anterior part of the posterior limb was slightly involved in an old hæmorrhage of moderate size which affected the thalamus mainly.

Thalamus.—The old hæmorrhage occupied the outer part of the thalamus and was of moderate size; another small area showed an almost complete absence of thalamic cells. The remainder of the cells of the thalamus appeared healthy except for pigmentation. A number of quite recent perivascular hæmorrhages were present on the inner wall of the thalamus adjoining the third ventricle.

Subthalamic region.—Perivascular hæmorrhages were prominent, especially around the third ventricle. A few of the vessels showed definite perivascular infiltration with small round cells. (An accident occurred to the Weigert-Pal blocks from the basal ganglia on the left side and also to the block from the subthalamic region, so that no Weigert-Pal sections were obtained from these regions.)

Mid-brain.—The substantia nigra showed no perceptible reduction in the number of cells on either side, though a slight degree of depigmentation had taken place. A few of the vessels showed inflammatory changes, but there was no evidence of glial cell proliferation.

Pons, medulla and *cervical* region of the cord showed no changes of note. Weigert-Pal sections of these regions showed, however, a slight but definite lesion of both pyramidal tracts.

Summary of Histological Findings in the Two Cases.

(1) In both cases subacute inflammatory changes were found; in Case 1 these were more prominent than in Case 2, and were most marked in the mesencephalon. In Case 2 the changes were slighter and were more evident in the basal ganglia and subthalamic region than in the mid-brain.

(2) In Case 1 there was a marked diminution of the cells of the substantia nigra on either side; in Case 2 the cells showed no reduction in number.

(3) The mode of death in both cases was strikingly similar, namely a sudden onset of pyrexia and tachypnœa *which were progressive.* Mlle. G. Lévy, in her recent book on the late manifestations of encephalitis lethargica, also describes this mode of death in four cases of advanced Parkinsonism. In neither of the two cases above described were

changes found in the medulla to account for the marked increase in the respiratory rate, and no signs were observed in the chest in either case during life sufficient to account for the tachypnœa. The perivascular hæmorrhages were similar in both cases and occurred in practically the same locality, i.e., around the third ventricle. It seems probable that these acute changes indicated a sudden flaring up of the morbid process, and that this was the immediate cause of death.

In both cases calcareous deposits were observed in the walls of the vessels in the anterior part of the globus pallidus and in this region only.

III.

Pathogenesis of Paralysis Agitans.

No attempt will be made here to discuss fully the pathogenesis of paralysis agitans. There are at present two opposing schools of thought. The one represented by the Vogts, Lhermitte, Ramsay Hunt and others, consider that the causative lesion in idiopathic paralysis agitans lies in the globus pallidus.

The other, led by Trétiakoff [13], who is supported by Pierre Marie, thinks that the symptomatology of this condition is dependent on disease of the substantia nigra. Trétiakoff bases his opinion on a close study of the substantia nigra in twenty-nine cases representing a variety of organic diseases, inflammatory and otherwise, of the central nervous system. In twenty of these cases he found no changes in this region. In all the cases of idiopathic paralysis agitans which he examined, numbering nine, he found degenerative changes in the substantia nigra; he further states that in the type of acute encephalitis lethargica characterized by katatonia he has found similar changes in this region. He also describes a case in which a unilateral lesion of the locus niger was accompanied by paralysis agitans affecting the limbs on the opposite side only.

Lhermitte and Cornil [10], on the other hand, in seven cases of disease other than paralysis agitans, i.e., combined sclerosis of specific origin, syringomyelia, cerebral tumour, two cases of complete section of the cervical region of the cord and senile dementia, state that they found alteration in the cells in the substantia nigra in all the cases. Trétiakoff, in reply to these criticisms, emphasizes the importance of three concomitant factors in such cases: (1) the physiological state of the patient; (2) the condition of the other systems of fibres, especially

the pyramidal system; (3) the time elapsing between the occurrence of the lesion and the death of the patient.

I have examined the substantia nigra in one case of each of the following diseases: myasthenia gravis, cerebral syphilis, subacute combined degeneration of the cord, primary dementia, myotonia atrophica, and recurrent cerebral hæmorrhage. In none of these cases did I find a diminution of the number of the cells, or depigmentation of pathological importance.

Three cases of idiopathic paralysis agitans were also examined from this point of view, and in all three cases a normal substantia nigra was found on both sides.

The substantia nigra in three cases of encephalitis lethargica, fatal in the acute stage, was found to be markedly affected; the reduction in the number of cells and the scattered masses of pigment being striking (fig. 6).

In Case 1, as previously described, the degenerative changes in the locus niger were very marked, and contrasted well with the relative paucity of the lesions in the globus pallidus.

In Case 2 the substantia nigra showed nothing abnormal beyond very slight depigmentation, and it is certain that the marked condition of rigidity which was present did not depend on a lesion in this region. I do not wish to emphasize this case as one of encephalitis lethargica in which the substantia nigra was normal. I am not certain that the paralysis agitans in this case depended on the attack of encephalitis lethargica, because large hæmorrhages, which were obviously due to primary arterial disease, were present in the basal ganglia on the right side and involved the globus pallidus.

In more than half the cases of the Parkinsonian syndrome following encephalitis lethargica which have come to autopsy, changes in the substantia nigra were definitely stated to be the most prominent pathological finding; moreover, in every case some degenerative change affecting the cells of the substantia nigra was found. Case 1 showed these changes in a marked degree.

We may surmise then that in idiopathic paralysis agitans a lesion of the globus pallidus, or possibly of the subthalamic structures with which it is connected, is the usual pathological basis of the disease; whereas post-encephalitic Parkinsonism is usually due to degeneration of the substantia nigra.

IV.

Calcification in Encephalitis Lethargica.

Buzzard and Greenfield [1] in 1918 were the first to note the occurrence of calcification in encephalitis lethargica. The case was that of a young woman of 28 who died six months after an acute attack of this disease. Calcification of a few vessels in the cortex, and more particularly of the vessels of the globus pallidus, was described by them.

Dürch [3] in 1921 found calcification in twelve out of fifteen fatal cases of encephalitis lethargica. The ages of the patients ranged from 30 to 60 years. Death occurred in one case as early as the eighth day.

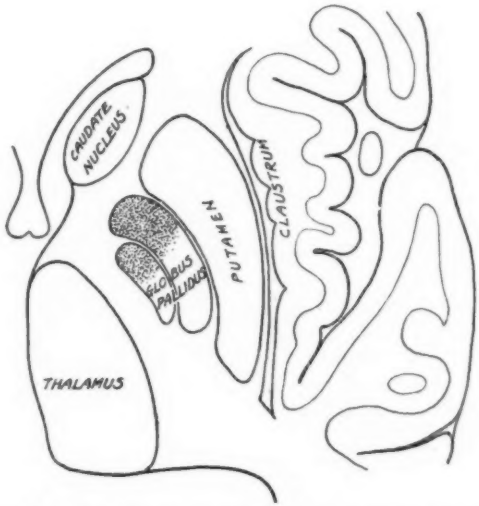

Fig. 5.—Diagram of basal ganglia. Dotted area indicates the region principally affected by calcification in encephalitis lethargica.

He described three forms of calcification: (1) calcification of vessels; (2) globules of calcium lying free in the supporting tissue; (3) calcification of nerve cells, this being the rarest form.

The calcification of vessels occurred most frequently in the corpus striatum, but also was found in the nucleus dentatus, hippocampus, cornu Ammonis, hemispheres and optic thalamus.

The calcified globules were most commonly observed in the hemi-

spheres, less often in the corpus striatum, and occasionally in the corpus callosum, gyrus hippocampi, optic thalamus and medulla oblongata.

I have examined the brains of six fatal cases of encephalitis lethargica, three dying in the acute stage and three a year or more after the original attack. In all six cases calcification in varying forms was found.

In all the cases, except one, the process was limited to the anterior part of the globus pallidus (fig. 5).

Case 1.—A case of paralysis agitans, has already been described fully. As previously mentioned the basal ganglia were cut horizontally into six slabs and numbered accordingly, No. 1 being uppermost, i.e., through the head of the caudate nucleus.

In sections from slab 4, i.e., through the middle of the globus pallidus, well marked calcification was found in the majority of the vessels in the anterior half of the globus pallidus. The vessels in this region in sections from slabs 3 and 5 showed hyaline degeneration, chiefly of the media, but no deposit of calcium salts in their walls. The cortex from several regions of the cerebellum and hemispheres was carefully examined, but no similar changes in the vessel walls were observed.

In addition to the change in the vessels, a number of mulberry shaped globules, staining dark brown with hæmatoxylin, were noted (Plate, figs. 1 and 3).

Case 2.—A case of paralysis agitans showed moderate calcification of vessels in the anterior half of the globus pallidus. This change was not present in sections from slab 6, i.e., the lowest part of the globus pallidus. No mulberry-shaped or calcified globules were observed, nor any fatty globules in frozen sections of the globus pallidus stained by Scharlach R.

Case 3.—Male, aged 20, was admitted to the National Hospital on December 29, 1922, under the care of Dr. J. Collier, to whom I am indebted for permission to publish the case.

According to his father the patient seemed in his ordinary good health until December 26, 1922, when he complained of feeling "out of sorts." He remained at home on the 27th and 28th, but he did not go to bed or complain of any further symptoms. On the morning of the 29th he was found by his father unconscious in bed and later he had a fit.

On admission to the National Hospital he was unconscious, but responded by movements of the limbs to painful stimuli. Breathing was stertorous. Salivation excessive. Temperature 102° F. Pulse 100. Respirations 30. The pupils were noted as small and reacted poorly to light. The right side of the face moved less well than the left. There was no paresis of the limbs. The arms were flexed and held rigidly across the chest. The deep reflexes were active; the abdominal reflexes were absent; the plantar response on each side was extensor in type.

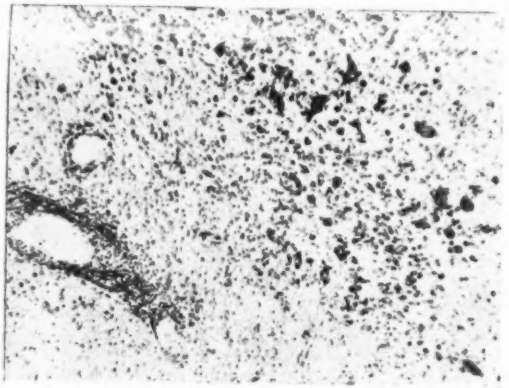

FIG. 6.—Photomicrograph × 100. Acute encephalitis lethargica. Section from mid-brain showing marked reduction in number of pigmented cells of substantia nigra and scattered masses of pigment.

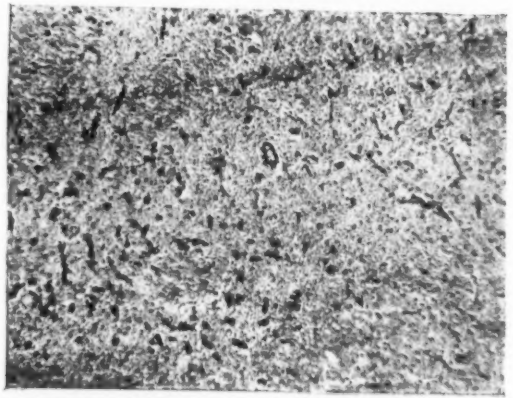

FIG. 8.—Photomicrograph × 80. *Case* 4. Acute encephalitis lethargica. Section from basal ganglia, stained with hæmatoxylin and van Gieson, showing calcified globules in globus pallidus.

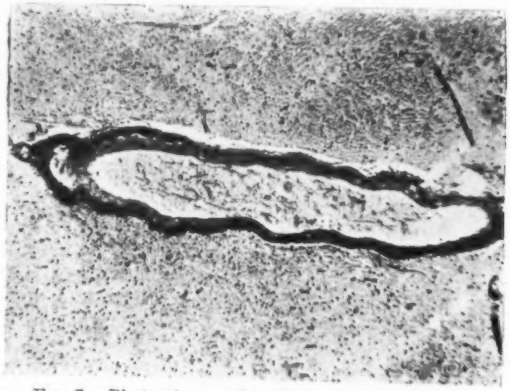

FIG. 7.—Photomicrograph × 80. *Case* 3. Acute case of encephalitis lethargica in a young man aged 20, death occurring on the fourth day. Calcification of a vessel in anterior part of globus pallidus.

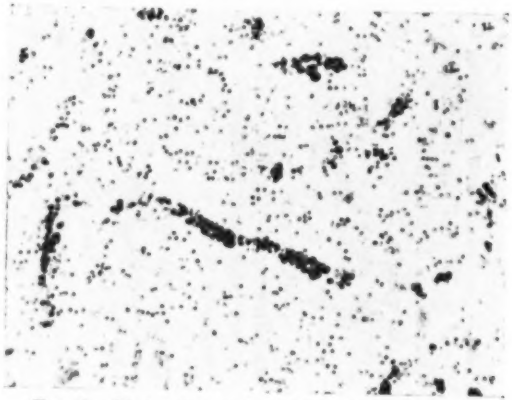

FIG. 9.—Photomicrograph × 160. *Case* 5. Chronic case of encephalitis lethargica. Calcified globules in globus pallidus.

At 8 p.m. on the 29th he had a generalized convulsion and another at 1 a.m. on the 30th. He died during the course of that day.

An autopsy showed typical findings of an acute encephalitic lethargica, namely, general vascular dilatation, perivascular hæmorrhages, and moderate round-celled infiltration. These changes were much more marked in the basal ganglia and cortex generally than elsewhere. The mid-brain showed very few changes, and the substantia nigra was normal.

In addition to these findings certain changes were present in the anterior half of the globus pallidus, namely: (1) hyaline degeneration of the vessels mainly affecting the media; (2) early calcification in a number of the arteries and arterioles (fig. 7 and Plate, fig. 5); (3) mulberry globules, similar to those mentioned in Case 1 (Plate, figs. 1 and 3). Sections from the cerebellum and cerebral cortex showed no similar affection of the vessels.

Case 4 was a case of encephalitis lethargica in which death occurred in the acute stage. Unfortunately all details of the illness are missing and cannot be traced.

The histological findings were as follows: Well marked inflammatory changes typical of acute encephalitis lethargica, i.e., general vascular infiltration with round cells and typical "cuffing." These changes were present in cortex, cerebellum, basal ganglia, brain-stem and cord, but were most marked in the mid-brain. There was considerable destruction of the cells of the substantia nigra. In addition to these findings there was present calcification of vessels in the anterior part of the globus pallidus and to a less extent in the cerebellum.

In the globus pallidus were seen calcified granules of small size, lying free in the supporting tissues and ranged along the capillary walls (fig. 8). In frozen sections from the basal ganglia on the opposite side, stained with Scharlach R., the earliest stage of these globules could be seen in the form of fatty globules. These were confined to the anterior half of the globus pallidus. (Plate, figs. 1 and 2.)

Case 5.—The histological investigation of this case was carried out by Dr. J. P. Martin, to whom I am much indebted for permission to examine his sections.

Female, aged 25, was admitted to the National Hospital in April, 1921. In April, 1920, she had an attack of encephalitis lethargica. She improved slowly, but in August of the same year she commenced to have repeated tonic contractions of certain muscles of the trunk, and these persisted.

On examination she showed a somewhat expressionless face with a flexed posture of the arms, suggesting an early Parkinsonian syndrome. The respiratory rate was constantly increased and averaged 40 to the minute.

In addition she had constant involuntary movements of both shoulders, the left being more affected than the right. The movements were due to spasmodic contraction of the latissimus dorsi. During the last six weeks of the illness there was continued pyrexia. Death took place on June 18, 1921.

The principal histological findings were as follows: (1) The mid-brain showed no changes of note beyond slight depigmentation of the substantia nigra and a slight reduction in the number of cells. (2) The subthalamic region showed a number of recent perivascular hæmorrhages in the region of the third ventricle; these were similar in all respects to those found in cases 1 and 2. (3) The basal ganglia presented no marked lesions except gross calcifications of the vessels and many calcified globules in anterior half of the globus pallidus (fig. 9 and Plate, figs. 1, 4 and 6). The cortex and cerebellum showed minimal changes, but no evidence of calcification was found elsewhere than in the globus pallidus.

Case 6 was a child, aged 7, who died on the tenth day of an acute attack of chorea, which may have been a manifestation of encephalitis lethargica. In the brain, in addition to mild inflammatory changes, there was definite calcification of a few medium-sized arteries in the anterior part of the globus pallidus, and mulberry globules in the putamen and globus pallidus. The vessels of the cortex of the hemispheres and cerebellum showed no calcification.

As controls for the occurrence of calcification in the globus pallidus brains of persons dead with the following conditions were examined: An accident, cerebral tumour (two cases), sub-acute combined degeneration of the cord, transverse lesion of the cord in the cervical region, Huntington's chorea, and three cases of idiopathic paralysis agitans.

In the case of Huntington's chorea well-marked calcification of vessels was found in the anterior part of the globus pallidus, but in no other situation; mulberry globules were also observed in the basal ganglia.

In all three cases of idiopathic paralysis agitans there was calcification of the vessels in anterior part of the globus pallidus. In none of the other cases examined were such changes seen.

The Vogts in their latest monograph on diseases due to pathological changes in the basal ganglia make mention of only one case showing calcification of vessels and of globules such as were present in the cases described above. This was a case of Westphal's, who died in 1918 after a seven weeks' illness characterized by athetotic movements, and later by dysarthria, dysphagia, retropulsion and general rigidity. The history and photomicrographs strongly suggest an attack of encephalitis lethargica, although no mention is made of this diagnosis in the text.

From the findings in the six cases described above it is evident that calcification occurs almost constantly in the globus pallidus in acute and chronic cases of encephalitis lethargica. In all six cases calcification of the vessels was observed, and in five out of the six cases globules,

either fatty, or in mulberry form, or fully calcified, were seen. Further, it must be emphasized that these changes were localized in every case except one (No. 4) to the anterior half of the globus pallidus, which area is supplied by internal striate branches of the middle cerebral artery. These changes will now be considered more fully.

Calcification of Vessels.

This may appear at a very early stage of encephalitis lethargica, i.e., on the fourth day of the illness in Case 4. Dürch [3] found the condition present in a patient who died on the eighth day.

Age seems to play no part in its production, as Case 6 was aged seven, and two of the other cases were under the age of thirty years.

The changes in the vessel wall preceding the deposition of calcium salts may be of two kinds: (1) a hyaline degeneration chiefly of the media, which becomes swollen and loses some of its nuclei; (2) a fatty degeneration of the vessel wall, the fatty globules appearing in the Virchow-Robin space, or more rarely in the media. These processes do not as a rule occur together in the same vessel, hyaline degeneration being the commonest.

The earliest deposits of calcium usually occur between the adventitia and the media. In vessels slightly affected the deposit may be seen in only a portion of the wall. The calcium is deposited in the form of granules uniformly small in size. The media is then invaded, and the granules coalesce to form solid plaques which entirely surround the vessel. The elastic lamina, in vessels in which the process is advanced, may be broken up in places and the granules may be seen immediately under the intima, but this is rare and the intima is usually spared. In addition to the deposit between the adventitia and the media, and in the media itself, vessels are sometimes seen surrounded by a number of small calcified granules which have invaded the Virchow-Robin space.

The lumen of the vessel is as a rule unaltered. One vessel in Case 5 was seen to be thrombosed, and the thrombus consisted entirely of calcium salts. Arteries and capillaries of all sizes may be affected; the veins less constantly show this change. There is rarely a concomitant perivascular infiltration of the vessels with round cells.

Fat globules.—In only one case (Case 4) was an opportunity afforded to study the earliest stages in the formation of these calcified globules. This was a case in which death occurred during the acute stages of the disease.

In frozen sections of the basal ganglia stained with Scharlach R., a

large number of fatty globules were seen in the anterior half of the globus pallidus. No other parts of the basal ganglia were thus affected. These globules varied considerably in size from 1-2 μ up to 20 μ or more. They lay free in the supporting tissue; many were aggregated along the walls of the capillaries. About half the number of globules seen were solid; the remainder showed varying degrees of vacuolation. The majority had a darker staining periphery (alum hæmatoxylin was used as a counterstain) and some in addition showed a second darkly staining ring in the substance of the globule, which gave it the appearance of possessing a nucleus. Most of the globules were round in form and were regular in outline. Some showed a crenated edge, and in them more darkly staining portions were usually seen. In a few the fatty element staining with Scharlach R. was replaced almost entirely by a blue-black mass which stained with hæmatoxylin, and which presumably consisted of calcium salts. All intermediate stages in pigmentation of the fatty globules were observed (see Plate, figs. 1 and 2).

In celloidin sections from the basal ganglia of the opposite side in this case, fully formed calcified globules were seen in the globus pallidus (fig. 8).

An attempt was made to determine the nature of the fat composing the globules.

Methods.—(1) Frozen sections were stained with Scharlach R., osmic acid, and Nile-blue sulphate.

(2) Frozen sections submitted to the action of fat solvents, e.g., acetone, ether, xylol, were treated as above.

(3) Bell's modification of the Dietrich-Ciaccio method.

(4) Hæmatoxylin after mordanting with bichromate.

(5) Bichromate-osmic acid method.

(6) Behaviour in polarized light.

With Scharlach the globules stained well, but as previously described, varying degrees of pigmentation, commencing at the periphery of the globule, were seen.

The globules remained unaltered after treatment with fat solvents; an attempt was made to remove the pigmented outer ring of the globules by a 3 per cent. solution of acetic acid, but sections so treated showed the same resistance to the fat solvents mentioned.

The globules stained moderately well with osmic acid, the periphery of the globule always stained the most deeply. With the bichromate-osmic acid method, the same results were obtained.

With Nile-blue sulphate the globules stained pink, but this may have depended on the long formalin fixation.

Sections stained by Bell's method showed similar results to those stained simply by Scharlach R.

The globules in unstained and stained sections showed no double refraction with polarized light.

Conclusions.

It is evident from these results, many of which are contradictory, i.e., the behaviour of the globules in presence of fat solvents and polarized light, that we are here dealing with fat substances which differ in several ways from those occurring in morbid conditions in other parts of the body.

The globules seem to remain unaltered throughout the various tests. What is there in these globules which differs from other fatty deposits elsewhere? It would seem that the answer to this question lies in the presence of the pigmented envelope which surrounds the globules; this was sometimes observed as a mere ring, but many globules showed an extension of this process inwards (Plate, fig. 1). This protective covering probably prevents the contained fatty substance in the globule behaving as an ordinary fat when subjected to the usual tests.

Emrys-Roberts and Haig [4] have described in a recent paper the occurrence of similar pigmentary changes in fat globules which they have observed in the myocardium, kidney and liver in fatal cases of fulminating diphtheria and subacute septicæmia. They describe the fatty granules as occurring in cells undergoing degenerative changes; these globules then may leave the damaged cells and appear in the surrounding tissue. A further stage then occurs, namely an alteration in the fatty or lipoidal globules whereby a progressive loss of fatty contents is accompanied by a gradual deposition of pigment at the periphery of the globules; a shrinkage process follows, resulting in the formation of minute deeply pigmented spheroidal granules. They investigated the nature of the fat content of these globules by a large variety of methods and stated as a result of their findings that these bodies were present unaltered morphologically and functionally in all frozen and paraffin sections both stained and unstained.

The resemblance between the bodies described by these two observers and the fatty globules in encephalitis lethargica is striking, and it seems probable that we are dealing with a similar alteration

in the fatty contents of the globules and bodies, though there is no indication as far as I have observed that the fatty globules in encephalitis lethargica originate from degenerated cells.

Calcified globules.—In three of the six cases examined (1, 3, and 6), in sections stained by hæmatoxylin and van Gieson a number of globules were seen lying free in the supporting tissue in the anterior half of the globus pallidus, and in two of the cases also in other parts of the basal ganglia. These bodies stained varying shades of brown; some showed a blue-black nucleus. In shape they somewhat resembled a mulberry, and have already been referred to as mulberry globules (Plate, figs. 1 and 3). These bodies are formed by the fusion of several globules, and may be as large as 50 μ to 60 μ. Small single round globules, staining in a similar manner, may be seen lying along capillary walls. From the resemblance in size and shape to the fully calcified globules (*vide infra*), and also from the presence in some of them of a blue-black nucleus, it was thought that these mulberry bodies were possibly transitional forms between the fatty globules and the calcified globules, but it seems as likely that they may form an alternative process to the calcified globules.

The latter were found in two out of the six cases in sections stained by hæmatoxylin and van Gieson. In Case 4 the occurrence of fatty globules has already been described; in sections from the basal ganglia of the opposite side small fully calcified globules were seen lying free in the supporting tissue in a small area in the anterior half of the globus pallidus (fig. 8). In Case 5 similar globules, though more numerous, were found in the same part of the globus pallidus (fig. 9 and Plate, figs. 1 and 4). In both cases there was an accompanying calcification of the vessels. These globules stain homogeneously blue-black with hæmatoxylin; they occur singly as small globules 2μ to 15μ in diameter, or in large "knobby" masses 50 μ to 60 μ in size. The majority of the globules were seen to lie along the walls of the capillaries, and often as minute granules around the larger vessels.

The Occurrence of Calcification in the Brain in other Conditions.

In arteriosclerosis, especially the senile form, deposits of calcium salts in the media are not of uncommon occurrence. They also occur in corpora amylacea and in psammomatous tumours.

Dürch has found calcification of the cerebral vessels in the brain of an idiot. He refers to further cases published by Virchow, Schmincke,

and others, and particularly to three cases of fatal carbon monoxide poisoning which died between the fourth and eleventh day, reported by Herzog, who found calcification in the vessels in the lenticular nucleus and mulberry-shaped bodies lying free in the supporting tissue. He considered that hyaline degeneration preceded the deposit of calcium salts in the vessels.

Dürch and Weingarten have both observed calcification in the vessels of the corpus striatum in cases of malignant malaria.

Weimann [18] has lately reported a case of dementia of ten years duration in which calcification was so widespread as to affect even the vessels in the pons.

The Pathogenesis of Calcification in the Cerebral Vessels.

The characteristic staining reaction with hæmatoxylin was accepted as sufficient evidence that the deposit occurring in the vessel walls and as globules consisted of calcium salts. No other specific stain for calcium was used.

Weimann has made an exhaustive chemical study of this deposit. He points out that in material which has been in formalin for any length of time most of the specific calcium tests are negative; he attributes this to the action of formic acid on the calcium. He further states that these deposits give a positive iron reaction, while tests for amyloid substance and glycogen were negative. He considers that the deposit is allied to a colloid group, and represents a ground substance containing iron and fatty substances. He emphasizes the fact that the deposit of the calcium granules first appears in the lymph spaces of the vessel wall, and he agrees with Hoefmeister who thinks that the deposition of calcium depends on an excess of calcium salts in the blood. The chalk is held in solution by protective colloids; if the latter be precipitated, then they may attract calcium salts, this process being further helped by a lowered CO_2 content of the blood.

Conclusions.

Although of considerable interest histologically I do not think that these changes play an important part in the production of the symptoms of paralysis agitans for the following reasons: (1) the lumina of the vessels remained patent except in one vessel in a single case. Despite this probable result I could find no evidence of serious nutritional alteration in the cells in the neighbourhood of the affected vessels or globules. (2) In two cases showing choreiform movements, i.e., Case 6,

and a case of Huntington's chorea, well-marked calcification of the vessels in anterior part of the globus pallidus was found, but neither of these cases showed muscular rigidity or any evidence of alteration in the function of the large motor cells of the globus pallidus. (3) In Case 5, a chronic case of encephalitis lethargica, the chief clinical symptoms were involuntary movements; the degree of Parkinsonism in this case was extremely slight and may have been accounted for by the slight changes in the substantia nigra. On the other hand, the globus pallidus in this case showed a more advanced degree of calcification of vessels and more uncommon calcified globules than in any of the cases which presented the Parkinsonian syndrome in a marked degree.

Taking into consideration the facts mentioned by Weimann, and comparing the morbid process in encephalitis lethargica with that existing in those cases of carbon monoxide poisoning and malignant malaria in which calcification of vessels has been found, it seems evident that a toxic process, either of bacterial or gaseous origin, acts on the walls of the vessels and, either directly by causing a hyaline degeneration therein, or by so altering the tissue fluids circulating in the lymph spaces of the vessels that there is a modification in the normal state of the blood calcium, permits of a deposit of calcium salts within them. It seems probable that only this latter process could account for such a rapid deposit of calcium salts as has been shown to occur in acute cases of encephalitis lethargica. The selective action of the process on the vessels in the anterior portion of the globus pallidus I am unable to explain.

Summary.

An account is given of the histological findings in two cases of the Parkinsonian syndrome following encephalitis lethargica.

The most constant findings were subacute inflammatory changes and recent perivascular hæmorrhages. In one case the substantia nigra showed marked degenerative changes, and in the other this area appeared normal; but large hæmorrhages of arteriosclerotic origin in the basal ganglia considerably modify the negative findings in the substantia nigra in the second case. An account is given of fourteen similar cases reported in the literature, in all of which the substantia nigra was affected.

Calcification in the anterior part of the globus pallidus was found in six cases of encephalitis lethargica, in one case as early as the fourth day of the disease. The calcification was found both in the vessel

walls and in the form of globules; the occurrence of fat globules was noted in one case, and the relation between these and the calcified globules was studied.

A short account is given of other conditions in which calcification occurs in the brain, and the pathogenesis and significance of these changes are discussed.

I must express my gratitude to Dr. J. G. Greenfield, Pathologist to the National Hospital for the Paralysed and Epileptic, Queen Square, London, for his valuable advice and great kindness in placing at my disposal a considerable amount of the morbid material which was used; also to Dr. J. P. Martin for permission to examine his sections from Case 5, and lastly to the various members of the staff of the National Hospital for permission to use and publish the notes of the cases which had been under their care.

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DESCRIPTION OF PLATE.

Camera lucida drawings of sections from the basal ganglia, showing various forms of calcification which affect the anterior half of the globus pallidus.

Fig. 1.—× 600. Diagrammatically arranged. (A) Case 4, Scharlach R. and hæmatoxylin; fat globules, showing pigmentary changes, and calcification in one globule. (B) and (C), Hæmatoxylin and van Gieson; larger forms of mulberry and calcified globules from various cases.

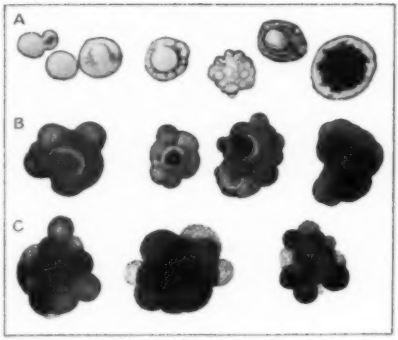
Fig. 2.—× 300. Case 4. Scharlach R. and hæmatoxylin. Fatty globules.

Fig. 3.—× 300. Case 3. Hæmatoxylin and van Gieson. Mulberry globules.

Fig. 4.—× 300. Case 5. Hæmatoxylin and van Gieson. Calcified globules.

Fig. 5.—× 250. Case 3. Hæmatoxylin and van Gieson. Early calcification in an artery.

Fig. 6.—× 250. Case 5. Hæmatoxylin and van Gieson. Calcification of vessels.



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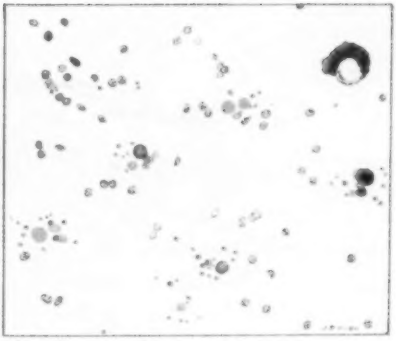

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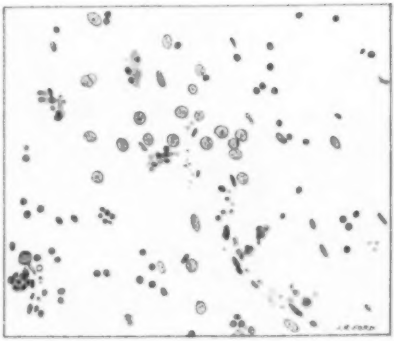

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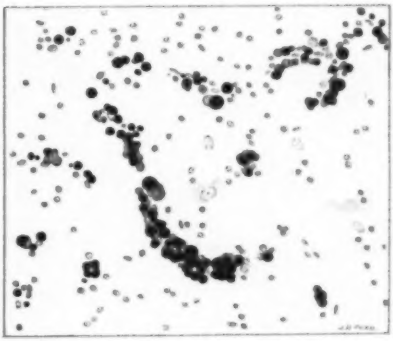

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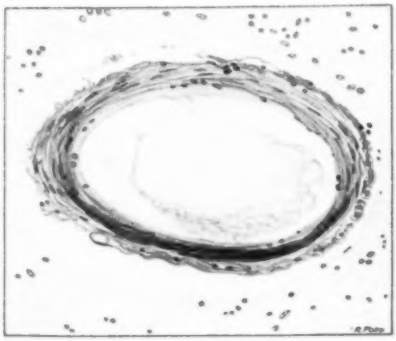

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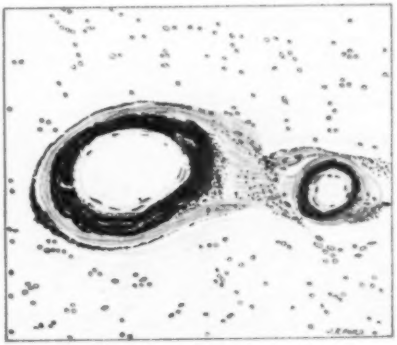

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ON VARIATIONS IN THE FORM OF REFLEX MOVEMENTS, NOTABLY THE BABINSKI PLANTAR RESPONSE, UNDER DIFFERENT DEGREES OF SPASTICITY AND UNDER THE INFLUENCE OF MAGNUS AND DE KLEIJN'S TONIC NECK REFLEX.

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CHAPTER I.—INTRODUCTION 281
CHAPTER II.—METHODS OF INVESTIGATION 283
CHAPTER III.—THE FLEXION REFLEX AND "EXTENSOR REBOUND" 284
CHAPTER IV.—THE TONIC NECK REFLEX AND THE FLEXION REFLEX: MODIFICATION OF THE BABINSKI PLANTAR RESPONSE ("REFLEX REVERSAL") .. 288
CHAPTER V.—CONCLUSIONS 297
BIBLIOGRAPHY 300

CHAPTER I.—INTRODUCTION.

WHEN the subject of a spastic residual hemiplegia firmly clenches the normal fist, the semiflexed and paralysed arm is seen to go into increased flexor hypertonus and to take up an attitude of increased flexion at the elbow until the voluntary grasp is relaxed, when it resumes its original posture and degree of spasticity. If now the patient be made to rotate his head towards the paralysed side and to repeat the experiment, it is found in many cases that the paralysed arm goes into tonic extension. In this simple observation we have an example of the modifying influence of one tonic reflex upon another, of a reflex arising in the proprioceptors of the neck upon one arising in those of the normal upper limb. In a recent paper [11], a series of tonic reflexes demonstrable in cases of hemiplegia was described and the study of their various modes of interaction led naturally to the question of interaction between postural and phasic reflexes, that is, between reflex postures and reflex movements. For example, is such a phasic reaction as the flexion reflex of the lower limb capable of modification in character under the influence of Magnus and de Kleijn's tonic neck reflex? Of particular interest is it to inquire whether the Babinski plantar response, which is a component of the flexion reflex, can be altered in form by

changes in head posture. On the general question of interaction between tonic and phasic reflex reactions, the whole weight of experimental evidence indicates that the co-ordination of movement, both voluntary and reflex, demands a continuous and close co-operation of the two, either as reinforcing or as antagonistic reactions. Clinical investigation, also, has thrown some light upon the matter. For example, the experimental and clinical study of the knee-jerk, which is a simple phasic reflex, has shown that the presence or absence of tone in the reacting muscle materially modifies the form of the jerk: Viets [8]; Gordon Holmes [4]. The "shortening reaction" which is appended to the jerk when this occurs in a spastic muscle represents an element in co-ordination of the greatest importance. In a previous study of the effects of a loss of postural tone upon co-ordinated movement, we saw that the abolition of this "shortening reaction" is a prime factor in the production of the gross disorders of movement we speak of as cerebellar ataxy [10]. On the clinical side, however, there have been no observations as to the influence of tonic upon phasic reflexes when the relationship between the two is one of antagonism. If we take the flexion reflex of the lower limb as our example, we have to determine whether its form and time relations vary under different degrees of extensor spasticity in the leg. There are two ways in which we may investigate this: either we can take a series of cases of hemiplegia, or of spastic paraplegia in extension, in which there are different degrees of extensor spasticity, and compare the form of the flexion reflex in each; or a more precise way is to determine the effect upon the latter of Magnus and de Kleijn's tonic neck reflex. Here we can pit two different grades of extensor hypertonus against a single, constant flexion reflex. The first method presents no practical difficulty, but it is less easy to determine the influence of head posture upon the flexion reflex, either of the upper or the lower limb, for while in the latter we have a readily obtainable and extensively studied flexion reflex, it is only in relatively rare instances that we can demonstrate the influence of head posture upon the lower limb. In the upper limb, on the other hand, where it is the rule to find some degree of tonic reflex action upon the limb, it is exceptional to find the phasic flexion reflex described by Riddoch and Buzzard [5]. However, cases presenting reflexes of both types, the tonic neck reflexes and phasic flexion reflexes, in both upper and lower limbs have come under observation and it has been possible by this means to confirm the observations made by the method of comparison from subject to subject.

In an earlier paper [9] a full account of the flexion reflex of the lower limb in man has been given, and evidence advanced showing that the so-called "extensor" or Babinski type of plantar response is an integral part of this reaction. Subsequent work by Head and Riddoch [3] has confirmed this view. It is possible, therefore, to employ the Babinski plantar response as an index of variations in the flexion reflex under the influence of different degrees of antagonistic muscle tone; a fact which lends a certain practical significance to the observations about to be recorded.

Chapter II.—Methods of Investigation.

Some method of graphic recording is essential to a systematic study of the flexion reflex, more particularly of that part of it known as the "extensor" plantar response. While variations of the latter in form and duration may be visible to simple observation, no analysis of them is possible, nor can variations from moment to moment or from subject to subject be accurately compared apart from some permanent record of the movement. The method and the apparatus employed have been described in earlier papers [9, 11], and only a few remarks are here necessary.

The stimulus adopted is that commonly in use for eliciting the plantar response, namely, stroking of the outer margin of the sole with a blunt object, in this case a metal rod. A band of fine metallic gauze, such as is used in "ionization" treatment, is fastened round the foot and placed in circuit with an electric signal. The stimulating rod is similarly connected and its moment and duration of contact with the sole are thus recorded on the kymograph surface. The latent period obtained by this means is only approximately accurate, for it is the application of the stimulus which is recorded, and not the moment at which it becomes effective. However, the method is sufficiently accurate for the purpose in hand and gives a good record of the length of after-discharge of the reflex and of the moment of onset of "extensor rebound." In the case of the flexion reflex of the upper limb, since a momentary pinprick is the best form of stimulus, a more precise record of the latent period can be obtained, for the stimulating needle comes in contact with the metallic gauze covering the hand at the same moment as it pierces the skin.

Chapter III.—The Flexion Reflex and "Extensor Rebound."

When we compare the flexion reflex obtained on stimulation of the sole of the foot in a case of paraplegia in flexion with that obtained from one of spastic residual hemiplegia or of paraplegia in extension, certain differences in form and duration are at once apparent. In the former case, the whole limb goes into full flexion with considerable force, while the foot and digits dorsiflex. The active flexion outlasts the stimulus, which may be quite momentary, and finally the limb may retain the attitude of flexion thus reached, or may subside passively into its initial posture of partial flexion. In the second type of case, where the lower limb is spastic in extension, the salient feature of reflex is the dorsiflexion of the great toe, the Babinski type of plantar response. To such an extent is this true that only within the past ten years have neurologists come to associate the response with limb flexion. Nevertheless, even when there is no visible excursion of limb at hip and knee, palpation of the hamstring tendons reveals contraction of these muscles as an invariable accompaniment of the Babinski plantar response.. Generally, however, there is some visible flexion at both hip and knee, but whatever its amplitude, the striking feature of this flexion of the limb is its transient duration and the quick and active return of the limb to the initial posture of extension.

If, then, we take the flexion reflex as a whole we find that the presence of extensor hypertonus diminishes its amplitude and cuts it short by a forceful and rapid return to the position of rest. In other words, the "after-discharge" characteristic of the unopposed flexion reflex is abolished by an "extensor rebound." If, on the other hand, we confine our attention to the dorsiflexion of the hallux, the effect of extensor hypertonus is much less striking, and requires for its appreciation the use of a graphic method. By this means, we find that the greater the degree of extensor hypertonus in the limb, the shorter the duration of the response; the shortening occurring on the return or extension phase.

The physiological principles underlying this influence of extensor hypertonus upon an intercurrent flexion reflex have been fully elucidated by Sherrington in the experimental animal, and his observations in this connection may be applied without qualification to the clinically observed phenomena. He says, "Many reflexes are intercurrent reactions, breaking in on a condition of neural equilibrium itself reflex. Take the case of the flexion reflex of the leg induced by a brief stimulus

during "decerebrate rigidity," where the animal may be regarded as a bulbo-spinal machine . . . If, then, the foot be excited by a brief stimulus and thus a flexion reflex induced in the limb, the limb is drawn up at hip, knee and ankle. The movement is brief; after being drawn up, the limb returns to its previous pendent posture. It is easy in many instances to perceive that the pose of extension, as resumed, is more marked than it was prior to the intercurrent reflex of flexion. It is also equally easy to perceive that in the replacement of the limb the extension is not a mere passive drop under gravity, but is a reversion to the previous posture by an active movement . . . There is an *active* reflex return to the pre-existing pose . . . When the flexion reflex disturbed the neural equilibrium it dispossessed the opposed reflex of extension from certain final paths common to that and itself. In other words, its own reaction induces an after-coming reflex antagonistic to itself" [6]. Further, not only is reflex tonic extension restored, but it may be increased in intensity. This increase depends upon the fact that "the intercalated flexion reflex lowers the threshold for the after-coming extension reflexes . . . *during* the flexion reflex the extensor arcs were inhibited; *after* the flexion reflex these arcs are in this case evidently in a phase of exalted excitability" [6]. Sherrington speaks of this condition as "post-inhibitory exaltation." It is a phenomenon to which we shall have again to refer. The simple cutting short of the dorsiflexion component of the flexion reflex is not the only effect of the presence of extensor hypertonus in the limb. Not infrequently in those cases where ankle clonus is elicitable, stroking the sole of the foot elicits a dorsiflexion of the foot and toe followed at once, or accompanied, by a spontaneous ankle clonus which persists for from four to six seconds. The study of a series of graphic records shows that this clonus in some cases begins during the active dorsiflexion phase of the response, while in others it is not seen until the return or extension phase. There are two ways in which this phenomenon may be interpreted. Viets [8] has found that for the development of clonus there is an optimum grade of hypertonus, and that if by appropriate means extensor hypertonus be increased to this level a clonus will develop spontaneously. There are two ways in which extensor hypertonus may be increased when the flexion reflex is elicited. The active dorsiflexion of the foot suddenly increases the tension in the calf muscles, just as does the passive dorsiflexion employed in the normal method of eliciting clonus. Despite reciprocal inhibition, this sudden increase may bring the tone of the muscle to the level at which clonus

is produced. This is probably the explanation in those cases in which the clonus begins on the active dorsiflexion phase of the reflex (fig. 5). The second explanation is that the extensor rebound, following the the active dorsiflexion and cutting it short, may be accompanied by the post-inhibitory exaltation referred to above, and that the hypertonus may

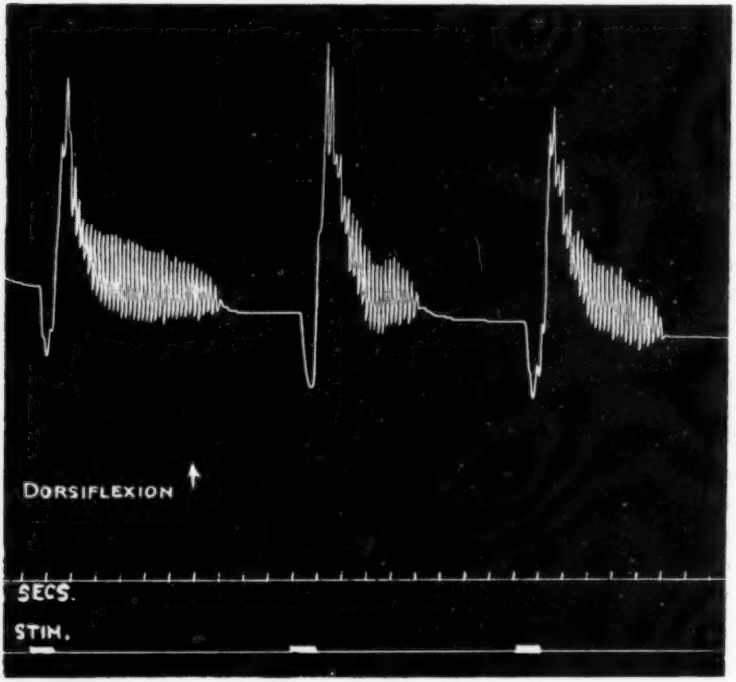


FIG. 1.—A series of three Babinski responses from a case of spastic paraplegia in extension (disseminated sclerosis). The dorsiflexion phase is preceded by a momentary plantarflexion. The extension or return phase of the response begins rapidly and during its course a spontaneous clonus develops. This lasts from four to six seconds and ceases with the foot and toe in the initial position of rest. In all figures, upward movement = dorsiflexion, and downward movement = plantarflexion. (1/1.)

in this way be brought to the optimum intensity for clonus. The cases in which clonus begins on the return or extension phase may possibly be explained in this way (figs. 1 and 2). In any case, whether or not the first explanation holds for both types, it is clear that the appearance of clonus is the result of a high degree of extensor hypertonus in

the reacting limb and is a modification of the plantar response attributable to this cause.

In addition, these figures reveal another interesting feature of the plantar response, which has been already referred to in an earlier paper [9], and is not rarely seen when there is a high grade of extensor spasticity in the limb. It consists in a preliminary plantarflexion of the great toe, upon which the dorsiflexion follows immediately. Simultaneous records of hallux and limb movements indicate clearly that this plantarflexion also precedes the flexion at hip and knee. Babinski has quoted the occasional occurrence of plantarflexion of the great toe in association with reflex flexion of the limb in support of the thesis that the dorsiflexor plantar response is a reflex distinct and separable from

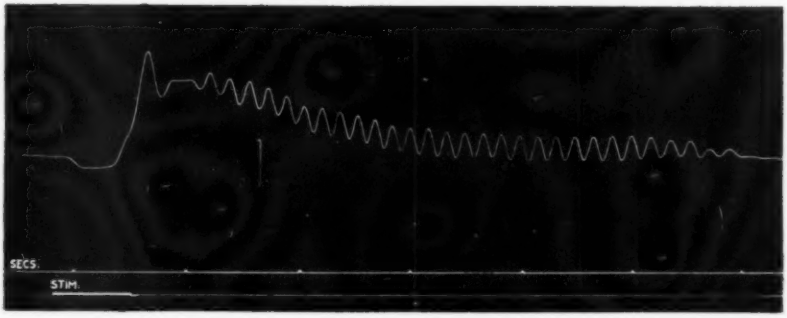


FIG. 2.—A similar record from the same patient taken on a rapidly moving surface. The development of clonus in the extension or return phase of the response is seen. (Reduced to 1/3.)

the flexion reflex. As the records clearly indicate, the argument is illusory and serves but to show the necessity of graphic methods of investigation in the case of rapid reflex movements.

In a re-statement of his views on this point [1], Babinski has again referred to this phenomenon, and it is necessary, in consequence, to indicate anew its relation to the flexion reflex.

To summarize, we may say that taking the flexion reflex as a whole, the presence of hypertonus in the limb extensors profoundly alters the amplitude and duration of the reflex, so that the dorsiflexor component becomes the salient and sometimes the only visible feature of the reflex. It does this in virtue of extensor rebound. The dorsiflexor component is much less profoundly modified, partly on account of its inevitably smaller amplitude, and partly because its after-discharge is

less prolonged even when the reflex as a whole is unopposed, than is that of flexion at hip and knee. Nevertheless, even this part of the reflex is cut short by rebound. In addition, the sudden tension in the calf muscles produced by the active dorsiflexion of the foot may set up a clonus, which is just visible during the active dorsiflexion phase of the response and reaches its full amplitude only when the rebound is established and the foot and toe are in active plantar-flexion. In some cases, clonus appears only on the return phase, and may then be regarded as possibly a manifestation of post-inhibitory exaltation of the extensor hypertonus. Finally, the dorsiflexion of foot and toe may be preceded by a transient plantarflexion. Since the latter also precedes the flexion at hip and knee it affords no support to Babinski's contention that the plantarflexion is part of the flexion reflex and that the plantar response or dorsiflexion is a reflex distinct and separable from it.

Chapter IV.—The Flexion Reflexes of the Upper and Lower Limbs and the Tonic Neck Reflex: Modification of the Babinski Plantar Response ("Reflex Reversal").

In the preceding chapter we have studied the effect upon the phasic flexion reflex of the lower limb of different degrees of extensor hypertonus. This necessitated the comparative study of the reflex in a series of cases. By means of Magnus and de Kleijn's tonic neck reflex we are able to produce variations in hypertonus in a single subject, at will, by the simple device of rotating his head towards or away from the hemiplegic side. It is true that so far as the lower limb is concerned we can do this in certain cases only, but, given a suitable subject, it is clear that we can examine the accuracy of the conclusions reached in the preceding chapter under very favourable conditions, for we are dealing with a constant flexion reflex which we can study against a background of at least two grades of antagonistic hypertonus. In short, the investigation of the influence of the tonic neck reflex upon the flexion reflex is simply an amplification of the observations already undertaken, and the results obtained are found to be strictly in accord with those described in the last chapter.

Figs. 3 and 4 record the dorsiflexion component of the flexion reflex (that is, the plantar response) in two cases of spastic residual hemiplegia in which the influence of the tonic neck reflex was just demonstrable in the leg. In each case, if the limb were supported by the observer while

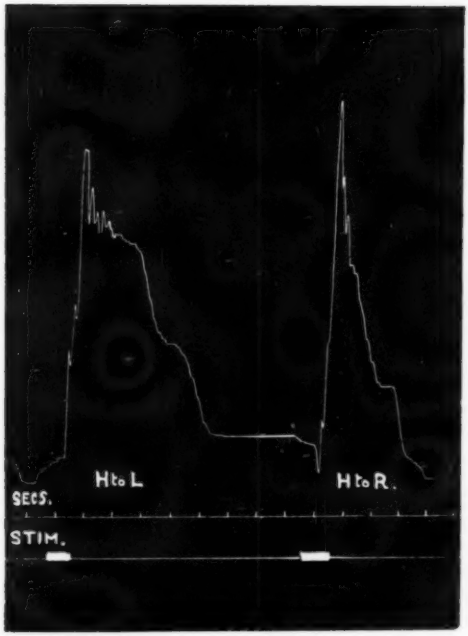


FIG. 3.—Two consecutive Babinski responses from a patient with right hemiplegia. With the head turned away from the paralysed side, the extension phase of the response is seen to be prolonged and the return to the initial position incomplete. With the head turned to the paralysed side, the extension phase of the response is appreciably shorter and the return complete. (1/1.)

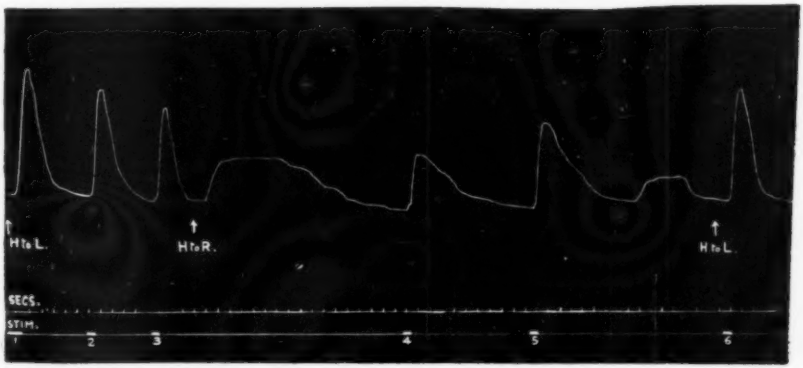


FIG. 4.—A series of seven consecutive Babinski responses from a patient with left hemiplegia. With the head rotated towards the left, the responses are cut short by extensor rebound (responses 1, 2, 3, 7). With the head rotated to the right the responses are strikingly prolonged in the extension or return phase (responses 4, 5, 6), and in the sixth response a second dorsiflexion occurs after the return to rest. (Reduced to 1/3.)

the patient voluntarily rotated his head through an angle of 180 degrees from the normal towards the paralysed side, it could be felt to become more spastic in extension. In fig. 3 are recorded two consecutive responses from one of these cases. The first was obtained with the subject's head rotated towards the normal side (left). It shows a leisurely relaxation or extension phase, which terminates a little short of return to the initial position. The second was obtained after rotation

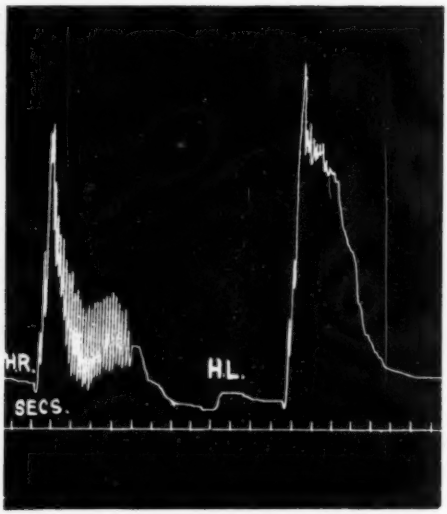


FIG. 5.—Two consecutive plantar responses. The first obtained with the subject's head turned towards the hemiplegic (right) side, the second with the head turned to the normal (left) side. In both responses two beats of the clonus are visible on the active dorsiflexor upstroke. In the first the return phase is rapid and clonus reaches a full development. The foot and toe return to a level just below that of the original base line. In the second, the return phase is more leisurely and is not quite complete. The clonus is minimal in range and duration. The difference between the two records depends upon the diminished intensity of extensor hypertonus of the limb at the time the second was taken, the diminution being the result of a tonic neck reflex (rotation of the head to the normal side). (1/1.)

of the head to the paralysed side (right). Here extensor rebound induces a rapid return or extension phase, which makes the whole response two seconds shorter than its predecessors, and which reaches a little below the base line from which the response began. In fig. 4 is a series of seven consecutive responses from a case of left hemiplegia. With the head turned towards the normal (right) side, the return phase is notably longer than when the head is turned to the

affected (left) side, the difference being a matter of several seconds. In this series, the prolonged responses were less ample than the shorter ones, but this finding was not invariable for this or other subjects. In a third case, the plantar response was accompanied by ankle clonus, which made its appearance during the active dorsiflexion movement, but reached its full development only during the return or plantar-flexion phase. With the subject's head rotated towards the hemiplegic (right) side, an ample clonus is seen during the extension (plantar-flexion) phase, but with the head turned towards the normal (left) side, the dorsiflexion is more ample, the return is delayed and the clonus is minimal. (Fig. 5.)

In two patients in whom well-developed tonic neck reflexes were present in both upper and lower limbs, even more striking modifications of reflex movements were demonstrable.

R. S., a seaman, aged 27, was admitted to hospital with a history of having received a blow on the right side of the head two years previously. He had been rendered unconscious, in which condition he had been trephined in the right parieto-occipital region. Both injury and operation occurred in Antwerp and no details of either are available. His present state (March, 1923) is that he has a spastic left hemiplegia of some severity. The arm is held flexed and adducted and retains relatively little voluntary power. He walks with extended leg and drags the foot. There is complete left homonymous hemianopia, but no impairment of acuity for any form of sensation. There is, however, a marked emotional overaction to painful stimuli applied to the left half of the body, and in the case of the arm a brisk flexion reflex accompanies pin prick or pinching (*vide infra*). The left tendon jerks are very brisk, there is ankle clonus on this side, the left abdominal reflexes are absent, and the left plantar is of the Babinski type, with slight rapid flexion at hip and knee. The spasticity of the left limbs is marked. Certain reflex reactions in the affected limbs may now be described at greater length.

Tonic neck reflexes.—With the patient lying on his back, rotation of the head to the normal side is followed by a slightly increased flexion posture of the arm (which is slung) and by slight active flexion of the supported leg, both of which are tonically maintained. Rotation of the head to the paralysed (left) side is followed by very slight extension of the arm due to diminution of the pre-existent degree of flexor hypertonus, and by increased extensor hypertonus in the leg.

Tonic neck reflexes and associated reaction.—On grasping with the normal hand, the following reactions are observed: Head in centre = flexion adduction of the arm. Head to left = extension-abduction of the arm. Head to right = flexion of the arm. A corresponding but less forceful and ample reaction is observed in the hemiplegic leg.

Phasic flexion reflex of the upper limb (left).—Pricking or pinching of the

skin of the upper limb anywhere below the level of the insertion of deltoid, or of the skin covering pectoralis major and the axilla, gives a brisk movement of flexion-adduction of the limb. The latency of this is 0·04 second. The response is the same in form from whatever part of the receptive field it is elicited.

Phasic flexion reflex of upper limb and tonic neck reflex.—The response described above is obtained with the patient lying on his back, the head in the

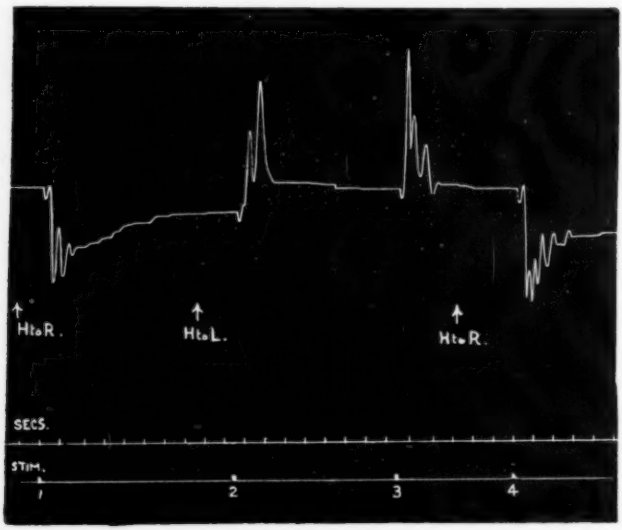


FIG. 6.—A series of four reflex movements from the upper limb in a case of left hemiplegia. The first and fourth consist in a flexion-adduction movement, that is, a movement employing the spastic flexors of the limb, and show marked tonic prolongation and shortening reaction. They were obtained with the head rotated to the right (normal) side. The second and third reflexes were obtained with the head rotated to the left (hemiplegic) side, and consist in a rapid movement of extension-abduction of the limb, without shortening reaction or tonic prolongation. The striking difference between the two types of response can be seen by looking at the record upside down. Down movement = flexion. Upward movement = extension. (Reduced to 2/3.)

median position and the arm slung. With the head to the right (normal) side, the flexion is more marked and the forearm and hand shoot across the body towards the right shoulder. If the head be now rotated to the affected (left) side, *the response is reversed in form*, and becomes one of extension-abduction of the limb. The latency is unchanged, but the distinct and constant tonic prolongation and shortening reaction of the original flexion reflex are both lacking. These differences in direction and form are readily apparent in figs. 6 and 7, which were taken on different days, but still show the same essential features.

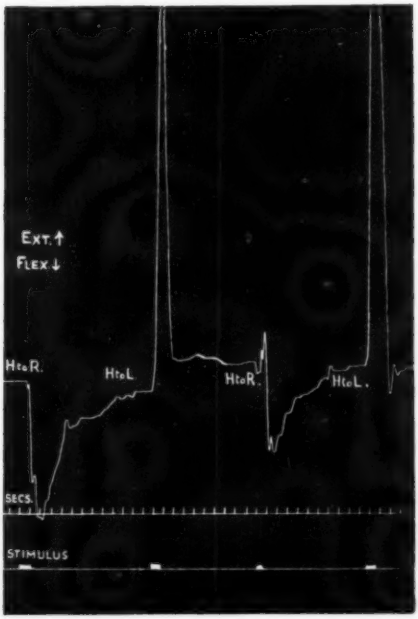


FIG. 7.—A similar record obtained from the same patient on another occasion. (Reduced to 2/3.)

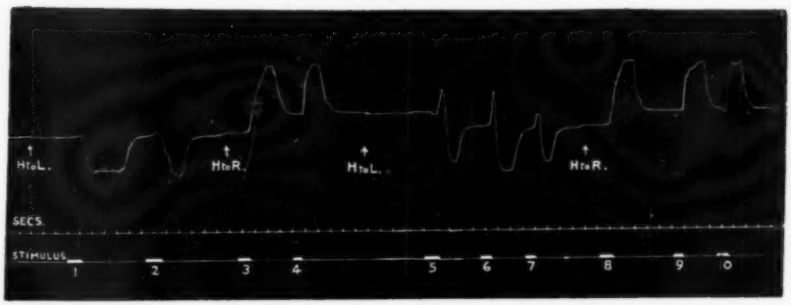
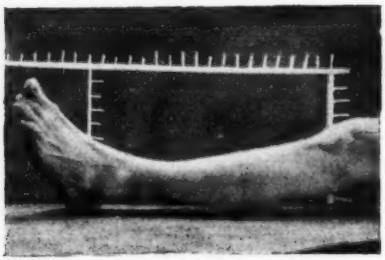
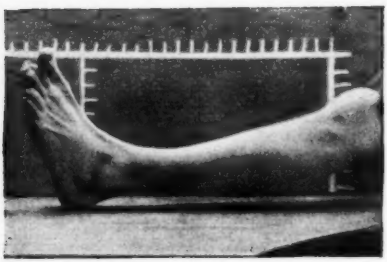


FIG. 8.—A series of plantar responses obtained with the head in the two lateral positions (Patient R. S.); 1, 2, 5, 6, 7, with the head turned towards the hemiplegic (left) side, and 3, 4, 8, 9, 10, with the head turned away from the hemiplegic side. The first two responses are completely plantarflexion, but the fifth, sixth, and seventh show an initial, diminished and very short-lived dorsiflexion (Babinski) response. Figs. 5, 6, and 7 were obtained from the same patient. (Reduced to 1/3.)

A



B



C

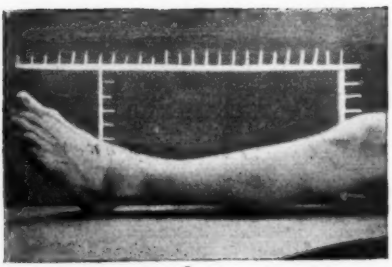


FIG. 9, A, B, C.—Three photographs from the patient R. S. A = the resting position of the left leg. B = the response to stimulation of the sole with the head rotated to the right. It consists of slight flexion at hip and knee with dorsiflexion of the foot and toe. C = the response to stimulation of the sole with the head rotated to the left (hemiplegic) side. This consists of a transient initial dorsiflexion of the hallux followed by active plantar-flexion of the foot and hallux, which is the phase here represented.

The scale marked on the background is in inches, and indicates the amplitude of the various movements.

This observation is of considerable physiological interest. By means of the tonic neck reflex the phenomenon of "reflex reversal" has been elicited, and as a result the relationship of phasic to tonic reflex changes from one of reinforcement (in the flexion reflex) to one of antagonism (in the extension-abduction reflex), with modifications in the form of the response which are visible in the records.

Flexion reflex of the lower limb and tonic neck reflex.—With the patient on his back and head rotated to the right (normal) side, the response to stroking the sole is a rapid slight flexion at hip and knee, the latter being lifted about three inches from the surface of the couch, and ample dorsiflexion of the foot and great toe. The average duration of the plantar component is three seconds. With the head rotated to the left (hemiplegic) side, the whole flexion reflex is altered. There is no visible flexion at hip or knee, and the plantar component consists of an extremely rapid and short-lived dorsiflexion of the great toe, lasting 0·8 second, and followed at once by ample plantarflexion of the foot and great toe. With mild degrees of stimulation there may be no initial dorsiflexion, uncomplicated plantarflexion occurring. However, increase in the strength of the stimulus always brings out the rapid, small dorsiflexion of the hallux. This finding was constant throughout a large series of examinations carried out over a period of several months (figs. 8 and 9).

A similar modification of the flexion reflex of the lower limb under the influence of changes in head posture was observed in a patient with a left hemiplegia, the subject of a cerebral tumour in the region of the third ventricle.

F. D., a woman, aged 24, was admitted to hospital with a six months' history of slight headache and occasional vomiting, and seven days' history of blindness of sudden onset. The patient was completely blind in both eyes from papillœdema and early secondary atrophy. No localizing signs were discovered. Following a right-sided decompression above the tentorium, she gradually lapsed into profound stupor and developed a left hemiplegia. In the course of two weeks, this became spastic and showed the characteristic attitude of the affected limbs and the usual reflex phenomena. In these circumstances, as the patient lay on her back in bed in a semi-conscious state, passive rotation of the head evoked well-marked tonic neck reflexes in both arm and leg. Rotation of the head to the left (hemiplegic) side was followed by active and maintained extension of the arm, and also of the leg if this were previously held in semiflexion by the observer. However, when the leg was already in extension, a marked plantarflexion of the foot followed and was maintained as long as the head remained turned to the left. *The flexion reflex of the lower limb* with the head rotated to the right (normal) side, consisted in slight flexion at hip and knee, with slow ample dorsiflexion of the foot and hallux. After the stimulus had ceased, the return to rest was incomplete, but if the head were now rotated to the left the foot and toe at once returned to their initial posture. With the head turned to the left (hemiplegic) side, the

flexion at hip and knee was much less ample, while the dorsiflexor component of the reflex was much shorter in duration, slightly reduced in amplitude, and was cut short by a quick extensor rebound. A series of these responses is seen in fig. 10. The modification produced by head rotation to the hemiplegic side is slightly different in character from that noted in the patient R.S., but is not less striking.

Several points of interest emerge from these observations. In respect of the flexion reflex of the upper limb, we see that the direction of a reflex movement may be reversed by a concurrent tonic reflex. Rotation of the subject's head towards the hemiplegic side tends to

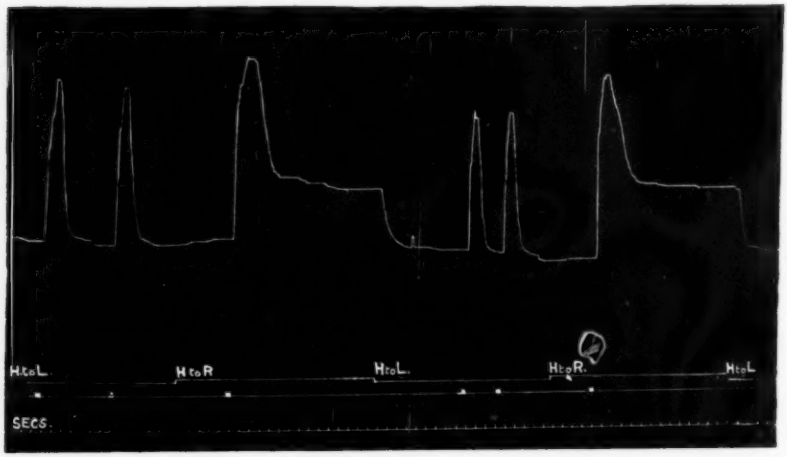


FIG. 10.—A series of six consecutive plantar responses from a case of left hemiplegia (Case F. D.) : 1, 2, 4, and 5 were obtained with the head turned towards the (hemiplegic) left side ; 3 and 6 with the head turned towards the (normal) right side. In the two latter the extension or return phase is prolonged and incomplete, but rotation of the head to the left (see upper signal) is at once followed by an active extension (plantarflexion) of foot and great toe to the initial position. (Reduced to 1/2.)

diminish the hypertonus of the limb flexors, so that now stimulation of the skin of the limb produces a reflex movement of extension. This "*reflex reversal*" is an example of a condition described by Graham Brown in the decerebrate animal, as resulting from the active assumption of a new posture by the reacting limb, and comes within the scope of the rule which he has formulated that "a stimulus which may throw into activity either of twin antagonistic centres (and depress the activity of the other) will tend to activate that which at the time is already in a state of relatively raised activity" [2]. More recently,

Socin and Storm van Leeuwen [7] have also described similar examples of reflex reversal in the decerebrate animal under the influence of Magnus and de Kleijn's tonic reflexes.

In the case of the lower limb, in the subject R.S. (Case 1) there is a similar but less pronounced tendency to reflex reversal, for with the head rotated towards the hemiplegic side the dorsiflexion component of the flexion reflex is seen to be constantly reduced in amplitude and duration, sometimes to be completely abolished, a plantarflexion (that is, an extension reflex movement) either cutting dorsiflexion short or replacing it.

It is interesting to recall that in their cases of reflex movement of the upper limb in hemiplegia, Riddoch and Buzzard found that in every subject but one the response was one of flexion. In the exception, extension was observed. Whether head posture played any part in the latter is an interesting matter for conjecture.

We may summarize the results described in this chapter as follows: In the case of the flexion reflexes of both upper and lower limbs, the active modification of the posture of the reacting limb by the tonic neck reflex tends to reverse the form of the reflex. In the case of the upper limb, this "reflex reversal" may be complete, but as seen in the lower limb it is incomplete and leads to diminution of amplitude and duration of the reflex. From the clinical point of view, we may express this tendency to reversal in respect of the Babinski plantar response and say that in certain cases of hemiplegia rotation of the head towards the affected side of the body alters the form of this response, and may even lead to its disappearance unless strong stimulation of the sole is employed.

In the case of the reversal of the flexion reflex of the upper limb, we have an example of a reflex movement employing muscles already engaged in a tonic reflex (flexor spasticity) being changed to one employing the antagonists of the spastic muscles (the extensors). In this way the relation of the two reflex reactions—phasic and tonic—is altered from one of reinforcement to one of antagonism. As a result the character of the reflex movement changes in the manner visible in the graphic records.

Chapter V.—Conclusions.

The observations recorded here raise several points of interest in the physiology of the nervous system, and demonstrate the essential similarity of the nervous processes governing the co-ordination of move-

ments of posture in man and the lower animals. In a previous paper we have seen that of the different tonic reflexes obtainable in certain cases of hemiplegia, one may profoundly influence the form of another which is synchronous with it. Thus, the associated flexion of the paralysed arm evoked by firm clenching of the normal hand may be converted into associated extension by a tonic neck reflex, produced by rotation of the subject's head towards the hemiplegic side. The present paper records observations made to determine whether certain of the reflex movements obtainable in man in spastic paralysis are also capable of modification by tonic reactions of this kind. The relationship of a tonic to a phasic reflex, i.e., of a reflex posture to a reflex movement, may be that of reinforcement or of antagonism. Clinically, the tonic prolongation of the knee-jerk in spastic paralysis is a familiar example of the former, but of the latter no examples have been precisely studied in man, although in animals Sherrington and others have analysed the result of such an antagonism. Clinically, the problem is readily investigated, for in the flexion reflex and the extensor spasticity of the lower limb we have a phasic and a tonic reflex respectively, employing antagonistic muscle groups—the flexors and dorsiflexors in the first case, and the extensors and plantarflexors in the second. We may, therefore, compare the form of the flexion reflex in a series of subjects with different grades of extensor spasticity in the limb. We may also study the flexion reflex in a single subject with the head in each of the two lateral positions (rotation to right and to left), that is, we may study it against a background of at least two grades of hypertonus. Further, since the Babinski type of plantar response is an integral part of the flexion reflex, of which it is the dorsiflexion component, we may use it as an index of variations in the form of the reflex. The main results of these observations may be expressed as follows: the presence of a high grade of extensor hypertonus reduces the amplitude and duration of the hip and knee flexion components of the flexion reflex very considerably. The Babinski plantar response component is less influenced, so that it may become the salient feature of the reaction. Nevertheless, this is also modified, particularly by the shortening of its duration. This cutting short and reduction of the flexion reflex is due to "extensor rebound," the nature of which is discussed. There may, however, be other manifestations than these. For example, the active dorsiflexion of the foot in the flexion reflex may, by the sudden increase of tension induced in the calf muscles, give rise to ankle clonus. In some cases the clonus makes its appearance during the active dorsi-

flexion, but does not reach its full development as long as the flexion reflex is in possession of the limb musculature. On the return of the extension phase, however, a full and ample clonus develops and lasts for some four to six seconds. In other cases, the clonus does not appear until the return phase is in progress. It is possible that here another factor is responsible. Rebound is known to be accompanied by an increased excitability, a "post-inhibitory exaltation" in the spasticity which has been transiently overset by the flexion reflex. This exaltation may, at certain levels of hypertonus, lead to the development of clonus in the manner described by Viets. Moreover, the marked depression of this clonus resulting from rotation of the head towards the normal side, as seen in fig. 5, shows that although tension on the calf muscles may be the stimulus producing clonus, yet the intensity of rebound is a further factor of importance. Probably both factors are at work in every case of clonus elicited in these circumstances. In those cases in which head rotation influences the degree of extensor tone in the lower limb, the same laws are seen to obtain, and in addition we may get an actual "reflex reversal" on stimulating the sole from the altered state of tone induced by the tonic neck reflex. When this reversal is not in question, rotation of the head towards the hemiplegic side increases hypertonus and thus leads to shortening of the Babinski component of the flexion reflex. Rotation of the head to the normal side lessens it and thus the response is appreciably lengthened. The lengthening occurs on the return phase and is due to a diminished intensity of extensor rebound. In those cases where clonus occurs in association with the plantar response, rotation of the head to the normal side may lead to its diminution almost to the point of extinction. One example of reflex reversal of the Babinski component of the flexion reflex is described. Here the dorsiflexion of foot and great toe is cut short before it reaches its full height and is at once followed by a slow and ample plantarflexion of both. To mild degrees of stimulation, the Babinski component may fail altogether, simple plantarflexion being the sole response.

One example of flexion reflex of the upper limb (Riddoch and Buzzard) came under observation, and here the influence of head rotation towards the paralysed side was completely to reverse the form of the reflex movement, changing it from one of flexion-adduction of the limb to one of extension-abduction. The circumstances in which this occurred and the principle underlying the change are those defined by Graham Brown as governing "reflex reversal" from the assumption

of a new active posture by the reacting limb. Another point of interest exemplified by this reversal is that in the reflex movement of flexion the spastic flexors were the prime movers and, therefore, the two types of reflex were allied in their activity. The reflex extension on the other hand employed the non-spastic extensors of the limb and, therefore, stood to the tonic reflex (flexor spasticity) in the relation of an antagonistic reflex. The modification in the character of the movement resulting from this alteration of relation is seen in the graphic records.

Finally, a practical point emerges, namely, that the Babinski type of plantar response may be diminished, or even abolished, by rotation of the head to the paralysed side of the body in hemiplegia. How often this phenomenon may be demonstrable, it remains for further experience to decide, but that it can occur at all suggests that it may be worth while, in cases where the plantar response is equivocal in form, to rotate the subject's head towards the opposite side when attempting to elicit the Babinski response.

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ON CEREBELLAR LOCALIZATION.

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A FEW years ago the writer, in a study principally devoted to the phylogenetic and ontogenetic development of the cerebellum [16], undertook to review the literature on the functions of the cerebellum and the localization of function within it. Anatomical and physiological considerations in connection with my own studies, and also with those of predecessors, induced me to put forth some principles concerning both the function of the cerebellum and the localization of the function in this organ. Since then several authors have discussed these same problems, and it has also become possible to consult works that were not available to me during the war. The following pages are intended as a further review of the progress made in these questions during the last few years. Two cases of cerebellar lesion that I have had the opportunity of observing in the Clinic of Internal Medicine, Lund University, will be used as a basis for this discussion. I take this occasion to extend to Professor Karl Petrén, as the head of this department, my thanks for his courtesy in giving me the chance of examining these cases.

Our knowledge of the cerebellum culminates in a few very important facts, all of which indicate that a great fundamental and uniform function is represented in this organ. The cerebellar cortex differs from the cerebral in showing no differences of histological structure. This statement means not only that all animals have the same layers of cells in the cerebellar cortex but also that the structure is the same in all parts of the cortex, even in the most intricate cerebellum, the human.

The second great principle in favour of this thesis is the fact that the cerebellum is built up in the same manner in all animals. Bolk has demonstrated this in mammals. In a study of cerebellar phylogenesis the writer was able to collect evidence to show that the cerebellum is constructed according to the same laws in the whole series of vertebrates

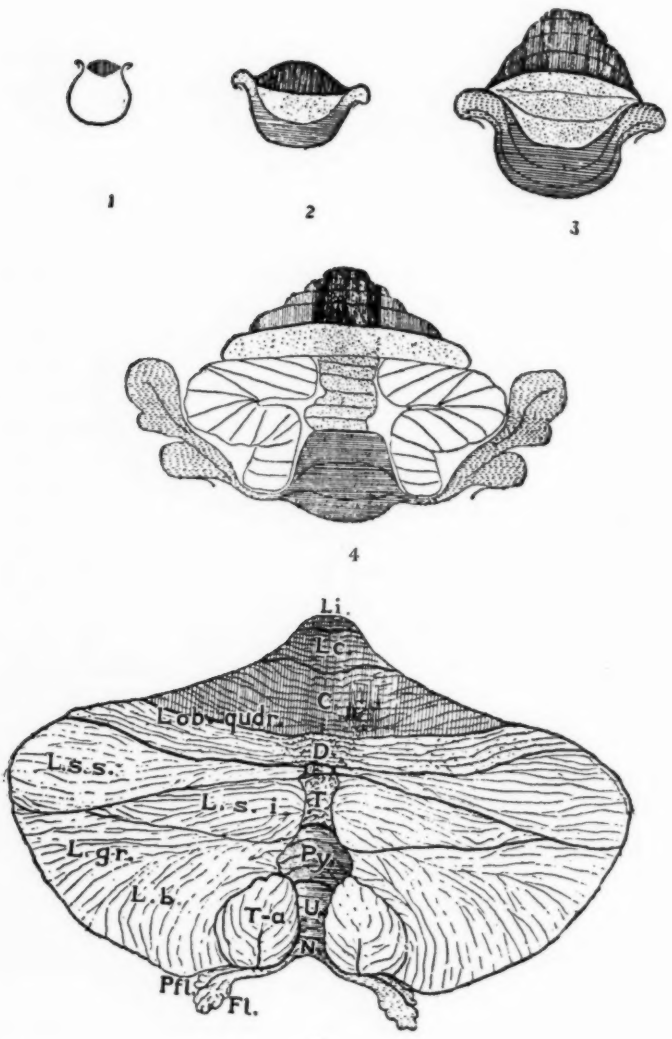

FIG. 1.—Diagrams of the cerebellum of (1) lacerta; (2) alligator; (3) bird; (4) mammal; (5) man; showing the homologies in the cerebellums of all these vertebrate classes. Vertical lines: lobus anterior. Horizontal lines and stipplings: lobus posterior. White area: lobus medius.

(fig. 1). The bony fishes cannot be included in this statement, because their development in this as in other respects seems to have gone its own way, but in the rest of the vertebrate series there seems to be a complete homology between the different parts of the organ, from the lowest to the highest. Thus, for instance, the alligator already has the same principal parts of the cerebellum as man.

The third great principle is that in all vertebrates without exception the cerebellum develops in the same place of the neuraxis. It cannot be a mere chance that the cerebellum always appears above the vestibular nerves. In lower vertebrates, such as petromyzon, it is a simple layer of cortical structure lying directly on the medullary nuclei of the eighth nerve, while in mammals fibres run directly from Scarpa's vestibular ganglion to the basal parts of its cortex. Thus the intimate relations of the cerebellum to the labyrinth are obvious.

Naturally, all these facts indicate a uniform function in all animals, and a uniform function in all parts of the cerebellar cortex, but they do not exclude a localization of function. As will be developed more fully below, there is a strong argument for localization in the distribution of the afferent fibres to the organ, since the different afferent tracts are distributed to different cortical regions. Such an arrangement must undoubtedly mean that in different regions different functions are localized. It must be assumed that the cortical function of a special region is brought into play only or mainly from a certain region of the body, and that the function irradiates from a certain area in the cerebellar cortex by the way of anatomical pathways only or mainly to special parts of the body. Thus we are not without anatomical indications of localization, even though they are scanty compared with the evidences of localization in the cerebral cortex.

The credit of the first important contribution to our knowledge of cerebellar localization must undoubtedly be given to the Dutch anatomist, Bolk. He was the first to study exhaustively the comparative anatomy of the mammalian cerebellum and to analyse its structure, which was a necessary preliminary to the investigation of localization within it.

Bolk divided the cerebellum into two parts, the lobus anterior and the lobus posterior, separated by a deep fissure, the sulcus primarius, which is a very conspicuous feature in all animals. The architecture of the lobus anterior is relatively simple and constant. The larger posterior part, owing to its more complicated structure, is also called lobulus complicatus. Its lateral parts, which form the lobulus anso-paramedianus, show the greatest variations.

The present writer (16) has found it necessary to criticize this subdivision of the organ into two parts. In my comparative studies of the cerebellum of all vertebrates I found an interesting parallelism between the most anterior and the most posterior parts of the organ. I therefore considered it necessary to divide the organ into *three parts*, a lobus anterior with the same limits as Bolk's anterior lobe, a lobus posterior, and between them a lobus medius.

It is necessary to emphasize in general terms the importance of this subdivision of the organ into at least three parts. No homogeneous sensory area in the nervous system ever develops by means of marginal appositions; the differentiation always takes place in the centre. The inferior olive, for instance, is in lower mammals a more or less plane disk, but as development places greater demands on its function it expands into a folded structure which reaches its highest development in the human brain. Even here its oldest parts are still those situated around the hilus, which would, if the olive were spread out in one plane, represent its periphery. That these parts are really the oldest from a phylogenetic point of view is indicated by the fact that in certain degenerative processes of the cerebellum, where the phylogenetically younger regions particularly suffer, all parts of the olive are affected except those around the hilus (Brouwer) [7]. Several other examples could be mentioned to prove this assertion. In this connection, it should not be forgotten that the same principle is found also in the architecture of the cerebral hemisphere. In lower vertebrates (frogs and alligators) this is related to the olfactory nerve and serves mainly as a centre for the sense of smell, and if the human hemisphere were spread in one plane it would be found that the whole area is bordered by the hippocampus, gyrus fornicatus, &c., that is, by the rhinencephalon. All anatomists (Kappers, Vogt, Brodmann, &c.) agree that these cortical areas are the oldest parts of the hemisphere. Within this original frame the magnificent vaulting of the hemisphere expands during the development. Next to the rhinencephalon, the cortical areas of the different senses are the oldest parts, and so far as their localization is known, we find them in the immediate neighbourhood of the cortex of rhinencephalon, the area striata or the visual area around the fissura calcarina, and the small gyri transversi or the auditory centre in the fissure of Sylvius (Flechsig, Henschen). In other words they also are situated in the borders of the hemisphere, and between them centres for the higher psychical functions appear. This is the general formula for the development and differentiation of the cerebral

hemisphere, as well as of every so-called sensory area of the nervous system.

The cerebellar cortex, with its uniform histological structure in all vertebrates, develops according to the same principles. In my comparative studies I found many signs that its marginal regions, that is the regions situated at the base of the organ immediately above the fourth ventricle, are the oldest parts from a phylogenetic point of view. They vary little during development, and their phylogenetic differentiation is very limited. They take no part in the intricate expansion found in higher mammals, the culmination of which is the building up of the human cerebellar hemispheres.

It is therefore necessary to consider the central parts of the cerebellar cortex separate from the border areas. As the cortex develops in an antero-posterior direction it will be necessary to divide the organ, from this point of view, into at least three parts, following each other from before backwards.

The anterior lobe must be given the same boundaries as described by Bolk. It forms the greatest part of the anterior vermis rostral to sulcus primarius. To the middle lobe belong mainly the two lobi ansoparamediani, i.e., the largest parts of the hemispheres. The posterior lobe consists of the most posterior segment of the vermis (pyramis, uvula and nodulus) and the floccular formations (flocculus and paraflocculus).

Therefore the limit between the middle and the posterior lobe is the sulcus præ-pyramidalis. I cannot recapitulate here all the arguments for the choosing of this borderline; I may only mention that it is indicated by certain characteristic features on the exterior of the organ. In many mammals (sheep and horse for instance) all lamellæ behind sulcus præ-pyramidalis have a much coarser architecture than the medial lamellæ lying in front of this fissure, indicating that the parts behind it must be regarded as a morphological unit in relation to the parts in front of it.

A study of the fibre connections of the cerebellum gives further support to the subdivision of the organ into three parts. The spino-cerebellar fibres, which reach the cerebellum by way of the tracts of Flechsig and Gowers, end almost exclusively in the anterior and the posterior lobes, whereas the middle lobe receives none. The termination of these fibres was at first studied by Horsley and Salusbury MacNalty [12], but, as I have pointed out in my first contribution on the cerebellum [16], it is difficult to get a clear idea from this work of the cortical

regions where they terminate. My own experimental studies on dogs and pigeons showed that the middle lobe is almost free from spino-cerebellar fibres.

Bremer [6] has recently corroborated this statement. By exciting the cerebellar cortex in cats with weak electric currents, he found two cortical areas from which inhibition of the extension of the extremities

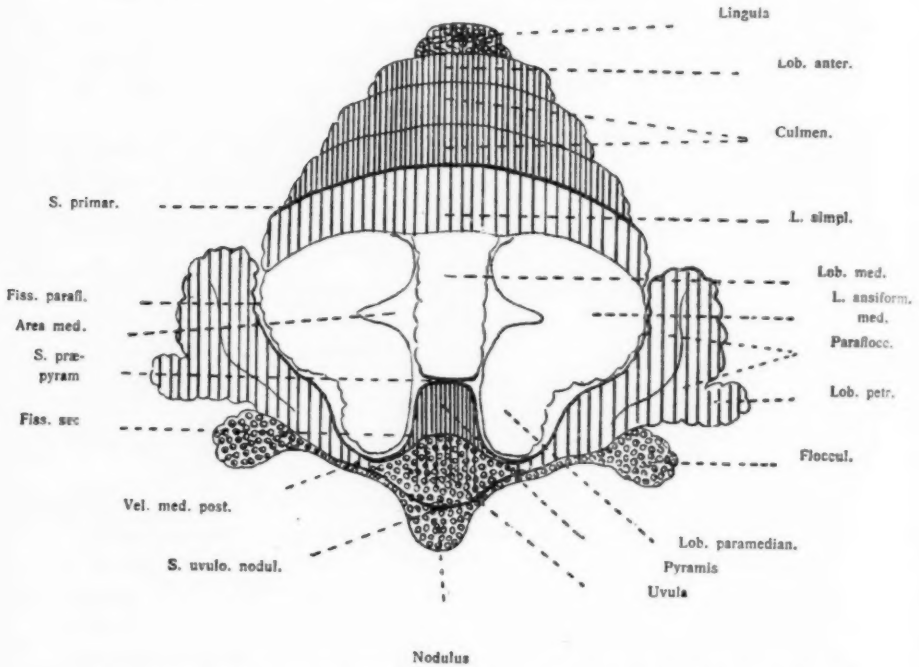

FIG. 2.—Diagram of the mammalian cerebellum, the cortex being spread into one plane. Vertical lines mark the endings of the spino-cerebellar tracts; circles mark endings of direct fibres from the vestibular nerves. The surface of the cerebellar cortex is conceived of as being spread in one plane; the periphery of the figure corresponds to the base of the organ, that is, those parts situated in the immediate vicinity of the fourth ventricle and especially of the vestibular nuclei.

could be elicited. Bremer writes: "The excitable zone has very distinct boundaries. In the anterior vermis it does not exceed the middle of the central lobe. The posterior boundary runs about one or two millimetres from the primary fissure. Another inhibitory area is found at the level of pyramis. These areas correspond exactly with the two regions where Ingvar has found that the spino-cerebellar tracts end."

The fact that anatomical and physiological evidence here agree is significant. We undoubtedly have in these two spinally innervated areas two fixed starting points for the further study of cerebellar localization.

Comolli and Edinger introduced the terms palæo-cerebellum and neo-cerebellum to indicate the different phylogenetic age of different regions of the organ. The oldest region, according to these authors, is the entire vermis and the flocculi, which they consequently termed the palæo-cerebellum. The rest of the organ, comprising the hemispheres and the lateral parts of the anterior lobe, was included in the neo-cerebellum. I have found it necessary to oppose this manner of subdivision, since many facts indicate that the vermis is not a morphological entity, and Bremer's physiological findings have corroborated this view. He has suggested that the anterior and posterior lobes (mihi) should be together called the palæo-cerebellum, and that the lobus medius (mihi) be designated the neo-cerebellum. I think this use of the significative and expressive terms is a happy one, and expresses the phylogenetic history of the organ more accurately than the system of Edinger and Comolli.

Marie, Foix and Alajouanine [24] are wrong in accusing me of having entirely rejected the conception of Edinger and Comolli of the palæo- and neo-cerebellum. I have only shown that it is not correct to regard the vermis as an anatomical and functional unit, running through the organ in a sagittal direction.

My subdivision of the cerebellum into three main lobes has been adopted by Kappers, Ransom, Bremer, and Marburg. I emphasize this point because of its great importance in the question of localization. It is impossible to have any idea of the functions of an organ until we have some knowledge of its structure. That experimental work on localization has failed to afford conclusive evidence is due to a large extent to the fact that the operators did not know, or did not pay attention to, the morphological subdivision of the organ. Parts considered as units have been excised which later investigations have shown to belong to different entities.

All these considerations cannot fail to have a great influence on our conception of the function of, and localization in, the cerebellum. In fact they form a most important key for a clear understanding of these important and difficult problems.

In considering the function of the middle lobe it is advisable to start with a consideration of our general knowledge of this region of the

cerebellum. The middle lobe is built up of the parts called by Bolk the lobuli ansiformis and paramedianus. These were shown by my own anatomical studies to appear first in mammals. They must be accordingly considered as the specific mammalian component of the cerebellum. They appear contemporaneously with the pons and the pyramidal tracts. The pontine fibres to the cerebellum are mainly connected with this middle lobe, and as the development of the pyramidal tract means a higher differentiation of motility, the development of the middle lobe of the cerebellum must also be related to regulation of the highest and youngest motor functions of mammals.

It is in these parts that a regional representation of the different sections of the body has been demonstrated. Bolk concluded from his anatomical studies that the lobi ansiformis and paramedianus must be functionally related to the activities of the extremities. He inferred that the anterior part of the ansiform lobe (*crus primum*) is related to the anterior extremity, while its posterior region, called *crus secundum*, has the same relation to the hind limb. His anatomical studies were succeeded by a long series of experimental observations by van Rhyneberk, Luna, Rossi, Lussana, Rothmann, Marrassini, Thomas, Durupt and Galante among others, all of which have confirmed his views of the arrangement of the centres for the anterior and posterior limbs in mammals.

It must be mentioned that Hesser and Troell [11] have raised doubts on this localization. They were unable to find evidence of any regional representation either within the middle lobe or in the whole cerebellum. After lesions of the anterior crus they found symptoms in the posterior limb and vice versa. Rossi, who must be considered as one of the most experienced workers on cerebellar physiology, has after a critical discussion of the symptoms following lesions in the middle lobe, concluded that there must be at least a prevalence of representation. In other words the fore-limb is related mainly but not exclusively to the anterior crus and the hind-limb mainly to the posterior crus and the paramedian lobe.

Altogether, almost all authors agree that the lateral parts of lobus medius, i.e., the hemispheres, are in functional relation with the extremities. So far the question of localization in the cerebellum seems to be settled.

There is no such agreement about the functions of the anterior and posterior lobes, but anatomical knowledge afforded by my studies has not failed to give valuable hints.

It seems reasonable to conclude that these parts, which have changed so little during phylogenetic development, have a fundamental function. Furthermore, the fact that these lobes receive the spino-cerebellar fibres, which originate from all segments of the spinal cord (Bing, Marburg) and are not segmentally represented in the cerebellar cortex, makes it highly probable that these regions have a function correlated to all spinal segments, that is the body or organism as a whole. But still more the fact that the anterior and posterior lobes receive fibres belonging to the vestibular nerves points in the same direction.

The most anterior parts of the anterior lobe and the most caudal parts of the posterior lobe are located in immediate vicinity to each other at the base of cerebellum and in proximity to the vestibular nuclei. That this is not accidental is shown by the fact that to these basal lamellæ (the lingula of the anterior lobe and the uvula, nodulus and flocculus of the posterior lobe) direct fibres go from the vestibular ganglia. I was able to show this experimentally by means of the Marchi method in the brain of a congenitally deaf cat, in which the vestibular nerve had been cut [16].

Valuable support is afforded to this view by the experimental observations of Greggio. After excision of the vestibular peripheral organs in new-born pigeons, he found a defective development of the cerebellum, particularly of its most posterior parts, that is of its basal lamellæ. Mesdag has in his ontogenetic studies of the brain of the fowl clearly demonstrated how vestibular fibres run only to the most posterior parts of the cerebellum.

These direct vestibular fibres suggest very strongly intimate vestibular relations of the basal regions of the cerebellum. A study of the functions of the peripheral vestibular organ and of the vestibular nerve may give us further insight into the possible function of these parts.

Of all the cerebellopetal fibres there are undoubtedly none of which the function is so well known as the vestibulo-cerebellar. The most prominent feature in the anatomy of the peripheral vestibular organs is the arrangement of the semicircular canals in the three planes of space. We also know that the clinical symptomatology of vestibular lesions is, as it were, connected with the different planes of space. Thus we find a lesion of the horizontal canal results in nystagmus which is mainly horizontal, past-pointing of the extremities in the horizontal plane, and lateropulsion of the body (Bárány). Any disturbance of a vertical canal produces vertical nystagmus, past-pointing in the vertical plane (upwards or downwards), and a tendency to fall

backwards or forwards, that is in the same vertical plane as the irritated canal. *There must be therefore a grouping of vestibular impulses in the central nervous system in relation to these planes.* Otherwise it would be impossible to explain the fact that the irritation of a vertical canal, for instance, produces vertical nystagmus, vertical past-pointing, and falling in the same plane. The vestibular impressions, acting on the mesencephalic motor apparatus for the eyes, as well as on the spinal motor apparatus for the extremities and the trunk, are grouped in relation to the planes of space, and this must necessarily also hold for the vestibular influence on the cerebellum. The vestibular innervation of the cerebellar cortex must therefore be arranged on the principle of the different planes of space. A similar view has been previously adopted by several authors (Ferrier, Hughlings Jackson). There are also, in fact, a few clinical observations which indicate that this is the case. Léri [23] concludes that each semicircular canal must be connected with a special region of the cerebellar cortex (compare p. 320).

This point of view also suggests that the functions of the cerebellum must in some way be related to the different planes of space. Many authors have studied symptoms of cerebellar disease from this aspect; Bárány has shown that certain deficiency symptoms due to cerebellar lesions, as past-pointing, are limited to certain planes, and the experimental observations of Thomas and Durupt show that the same principle holds in animals. It is an old observation that the falling in cerebellar lesions is mostly in one special direction, backwards, forwards, or to one side. The direction varies in different cases, but it is often constant in the same case during the whole period of the illness. From these facts it seems highly probable that the innervation of the cerebellum is related to the action of different synergic groups of muscles acting in one special direction, or in one plane of space.

It seems logical to expect such symptoms to result from disease of those parts of the cerebellar cortex that are innervated directly from the vestibular nerve. A lesion of these regions can to a certain extent be considered as a lesion of the vestibular nerve itself. In fact, after lesions of these parts very characteristic symptoms appear in the acute stage, the so-called forced movements which in many respects remind one of pure vestibular symptoms.

We know from physiological experiments that after lesions of the lateral parts of the cerebellum there appear certain motor phenomena known as "forced movements"; the animal falls towards the side of lesion, that is rotates around its own axis. This phenomenon increases

as the lateral peduncles are the more involved in the lesion. There is no agreement on the direction of falling, except that in the majority of the cases it is towards the side of the lesion, but it also occurs towards the opposite side. A tendency to fall forwards or backwards following lateral lesions is very seldom observed.

Forced movements in the sagittal plane, around a frontal axis of the body, are, on the other hand, a prominent feature after lesions of the medial part, i.e., the so-called vermis of the cerebellum.

In animals total experimental destruction of these medial regions offers great difficulties. The most anterior part of the vermis is situated in the cavity beneath the cerebellum, immediately above the fourth ventricle, and any attempt to remove the whole anterior lobe therefore involves the risk of injuring the medulla oblongata also. In fact a study of the majority of the records of operations on the lobus anterior shows that only its upper or more or less superficial parts had been damaged. The lobus posterior is more easily removed, but its most caudal part, the nodulus, is located very deeply, and it is only when special attention is paid to it that it can be extirpated with the rest of the lobus posterior. From our knowledge of the connections of the basal lamellæ it is evident that these parts must have very important functions. But as a rule these lamellæ are spared in experiments, owing to technical difficulties, and this may be the reason for many obscure and contradictory statements concerning forced movements in the experimental literature. For this reason also the work of Hesser and Troell [11] is hardly apt to give any elucidation of the question of the origin and the direction of forced movements in the sagittal plane, because these parts were not removed in any animal recorded by these authors.

In my studies on the basal parts of the cerebellum, I found that when the posterior lobe had been totally removed the animals showed a remarkable tendency to fall backwards, whereas in animals in which the anterior lobe had been removed quite other symptoms were observed. I therefore concluded that the synergies necessary for maintaining the body balance backwards were regulated in this part of the cerebellum.

A tendency to fall backwards has been observed by several operators on the cerebellum (Ferrier, Marrassini, Thomas and Rothmann), but there is no agreement as to the injury of which parts this phenomenon was due; some observers observed this symptom after lesions of lobus anterior. Russell [32] found that his animals fell backwards after ablation of pyramis, declivum and part of the monticulus. Rotation

movements were not observed in such animals, except in one instance when they occurred a few hours after operation and then were slight. When the greater part of the vermis, including the whole of the posterior half and some of the anterior, was extirpated, the tendency to fall backwards was slighter than when the posterior portion of this lobe alone was removed.

My own studies [16] confirmed Russell's results entirely. Recently Simonelli [33] has investigated this same question. In order to test my results he has removed in dogs, cats and rabbits, the posterior lobe, as I have described it. He summarized his results in the following manner: "After ablation of the posterior lobe there are to be seen dynamic phenomena of a mainly accessory type. They are characterized by dorsal extension of the head, extension of the anterior extremities, opisthotonos, falling backwards and crises of motor agitation." Only when the uvula and nodulus were removed did falling backwards appear. Lesions of the pyramis gave no such symptoms. From this it will be seen that the symptoms observed by Simonelli are the same as those described in my work, and so far I consider that this author has corroborated my observations. Simonelli, however, regards the backward falling of the animals as a so-called dynamic phenomenon, not as a deficiency symptom (compare p. 313). However, it must be considered as absolutely proven that after ablation of the most posterior parts of the cerebellum (the nodulus and the uvula) there appear in different animals immediately after the lesion motor phenomena characterized by a falling backwards. From no other part of the cerebellum can this phenomenon be elicited in the same manner.

From my own experiments and also from those of Simonelli it is clear that the falling backwards is most prominent when the uvula and nodulus are entirely destroyed. The fact that the falling backwards is elicited especially from those parts innervated by the vestibular nerve makes it very probable that the vestibular innervation plays some rôle in this phenomenon. This assumption is all the more probable since this falling backwards is very similar to that which appears after lesions of the vertical semicircular canal.

Simonelli has criticized my theory of cerebellar localization. In spite of the fact that he has found the same phenomena in his operated animals, he concludes that the posterior lobe has nothing to do with the falling backwards of the body. This paradox depends on Simonelli's interpretation of the falling backwards as a so-called *dynamic* symptom. Luciani was the first who termed these acute

motor phenomena which follow cerebellar lesions, i.e., the forced movements, dynamic. He concluded that they cannot be considered as genuine symptoms of cerebellar deficiency, but should be regarded as secondary in some way to vertiginous paroxysms due to irritation or paralysis of the cerebellar peduncles.

Simonelli expressly states that the falling backwards observed in his animals was certainly due directly to the cerebellar lesion. The fact that this phenomenon only persisted during the first days after the operation induces him to call it "accessory." And as a true adherent of Luciani he considers that it is without importance in our interpretation of the function of the posterior lobe.

It is clear without further discussion how arbitrary such an interpretation is. How is it possible to denounce the value of a symptom that is of cerebellar origin? It seems to me that Simonelli here has sacrificed too much to his loyalty to his great countryman. The fact that the dynamic phenomena appear only in the acute stage of the lesion does not entitle us to put them aside as valueless in the study of the cerebellar physiology. As it has been proven that destructions of the posterior lobe elicit most typically symptoms of falling backwards, we must ascribe to the posterior lobe the faculty of eliciting in some way the necessary muscular synergies that are necessary to bring about the falling backwards, even if this symptom persists only during the acute stage, and even if we do not know the reason why it disappears. We cannot afford to put them aside as valueless, as accessory. The difference of opinion between Simonelli and myself is thus merely a matter of interpretation.

As the dynamic phenomena seem to be more severe after injuries to those parts that are directly influenced by the vestibular nerve, these regions would seem promising ones for future study. The uniformity of the cerebellar cortex makes it highly probable that the organization of the function in all parts of the cerebellar cortex is identical. Thus if we are able to reveal the organization of the function of the basal parts we will have a key to an understanding of the whole cerebellum.

The experiments of Magnus and de Kleijn [22] on the relation of the vestibular organs to the attitude of the body and its different parts have shown that all these reactions (Stellungsreflexe, vestibular reflexes) persist after the removal of the cerebellum. Their conclusion is that the cerebellum can no longer be considered as the main organ of the vestibular nerve, as it has been in both anatomical and physiological

logical literature (Sherrington). Their observations do not refute what has been said above; they merely show that the reflex mechanism of body-attitude which is related to the vestibular apparatus is laid down in the medulla, mid-brain and spinal cord, as it were underneath the cerebellum. These authors leave the question open whether in an intact central nervous system vestibular impulses reach the cerebellum and take part in its function. The fact that Scarpa's ganglion sends fibres directly to the cerebellar cortex is too strong an argument in favour of the vestibular influence on the cerebellum to be neglected. Though great caution must be exercised in translating anatomical facts into physiological theories, if structure means anything we must insist upon the functional relationship between the vestibular nerves and the cerebellum. The work of Magnus and de Kleijn shows that the importance of vestibular influence on cerebellar function must not be overestimated, as there has been a tendency to do in both the anatomical and the physiological literature.

The cerebellum may be considered as a conglomerate of nervous tissue where impulses from different sources are correlated. The two most important sources of these impulses are undoubtedly the vestibular organs and the spino-cerebellar paths, but other cranial sensory nerves also contribute.

During phylogenesis there has been a tendency to regression of the vestibular organs and to further development of the spino-cerebellar pathways. Many signs indicate that the vestibular organs constitute a sense organ fitted for orientation in a fluid or gaseous medium (water and air); a dog from whom they have been removed will drown if thrown into water, but if the cerebellum only is removed he can swim. Human beings without a functioning vestibular apparatus never learn to swim. Fishes and birds have comparatively much greater peripheral vestibular organs than mammals, and especially than the higher animals. On the other hand the spino-cerebellar tracts increase in size during phylogenesis; fishes have spino-cerebellar fibres from the cervical segments only (Kappers), whereas in mammals they come also from the lowest segments of the cord (Bing, Marburg).

There are, therefore, grounds for the theory that during phylogenesis the influence of the labyrinth on the cerebellum diminishes, while that of the spino-cerebellar tract increases. Consequently, if impulses reaching the cerebellum from the exterior by the only two possible ways, vestibulo- and spino-cerebellar tracts, are elaborated here, the spino-cerebellar influences ought to play a more important part than

the vestibular in higher animals. This is in accordance with the findings and conclusions of Magnus and de Kleijn.

The theory of vestibular function now most generally accepted is that formulated by Mach, Breuer and Crum Brown, according to which the static and kinetic properties of the endolymph and the otoliths are the active stimuli of the peripheral vestibular apparatus. Since, according to this interpretation, the vestibular nerve conducts impulses initiated by static and kinetic changes in the vestibular organ, it is impulses of this nature that reach the basal regions of the cerebellum to which the vestibular fibres run directly.

This is in complete accordance with the old conception, first formulated by Magendie, of the cerebellum as an organ for the regulation of the equilibrium of the body. This function naturally cannot be limited to the static equilibrium of the body; it must also during motion regulate the different muscular activities concerned in dynamic equilibrium. I have, in my anatomical studies, declared myself an adherent of the view that the cerebellum is a reflex organ which preserves the static and dynamic equilibrium of the organism. This conception receives the strongest theoretical and logical support from the great uniform principles in the constitution of the cerebellum mentioned in the introduction to this article. It is in accordance with the anatomical and phylogenetical relations of the cerebellum and the vestibular nerves, and with our knowledge of the functions of the labyrinth. It explains better than any other hypothesis the great anatomical and histological uniformity of the cerebellum in the whole vertebrate series. It is also in accordance with the clinical symptoms of cerebellar disease.

As an organ regulating the static and dynamic equilibrium of the body masses it must, as I have pointed out [16], regulate muscle tone in the different regions of the body in all muscular activities. In 1918 I tried to interpret all the various clinical cerebellar symptoms as a disturbance of muscular tone, and to give a consistent explanation of cerebellar syndromes. So far as I know I was the first in this endeavour. Later Ramsay Hunt [15] and especially Walshe [38] and Holmes [14], have given explanations of the cerebellar symptoms, that in important parts are identical to mine and in other respects come very close to it. On the whole, it can be said that there has in later years been a general tendency in the literature to abandon the conception of Luciani, who divided cerebellar symptoms into atonic, astenic and astatic components. Even the Italian school has tried to consider the cerebellar syndromes from a more uniform point of view. So Rossi and Simonelli

[30] explain the astatic and most of the so-called astenic symptoms as a consequence of the atonia. There has since 1918 been a growing tendency to attempt a uniform explanation of all cerebellar symptoms and attribute them to a disturbance of one specific function. By many authors the cerebellum has been looked upon as the reflex organ for the co-ordination of the muscular activities. Gordon Holmes writes: "A fuller recognition of the part that the postural tone plays in both active and passive attitudes and in the movement has cut down enormously the symptoms in the explanation of which it is necessary to invoke incoordination."

Bolk concluded from his anatomical studies that the anterior lobe was related to the muscular functions of the head (the face, tongue, larynx, &c.), whereas the posterior lobe (mihi) was related to those of the trunk, and especially of the tail and perineum. My studies on the fibre connections make one doubtful about this system of localization. The fibre connections of the anterior and posterior lobes indicate strongly that the functions of these parts must be related to the body as a whole and not to any special segment of it.

I concluded further that the anterior lobe was related mainly to regulating the motor functions necessary to maintain the equilibrium of the body and preventing the body from falling forwards, whereas the posterior lobe played a rôle in maintaining the equilibrium backwards.

It is interesting to find that Gordon Holmes in his recent extensive studies on the clinical symptomatology of cerebellar lesions writes: "Certain facts indicate that there may be a further localization of function within the human vermis; I have for example observed a tendency to stagger backwards in tumours and other lesions of its posterior portion, and a falling forwards in one case at least of tumour in its anterior part."

According to this there is no regional representation of the body segments within the cerebellar cortex of the anterior and posterior lobes. That which is localized here is the complex of different synergies acting in equilibrium, according to the principle of the direction in the different spacial planes. In these parts the regulation of the synergies necessary for the static and dynamic equilibrium of the body as a whole is laid down.

The same principles can be applied to the middle lobe. Here it seems to be definitely proved that the anterior region (crus anterius) is related to the activities of the fore-limb, whereas the posterior part

(crus secundum) is related to the posterior limb. But also here the conception of the cerebellum as a regulating organ of muscular tone, in order to preserve and maintain the static and dynamic equilibrium of the body masses, is a strong objection against any definite regional representation of different body segments in its cortex. Only a prevalence of representation in the sense of Rossi would be in accordance with the above principles.

In later times several observations have been made that have been interpreted as unfavourable to all theories of localization. So Rossi [29] has stimulated the cerebellar cortex with electrical currents and thereby found that the excitability of the contralateral cerebral motor cortex is increased. If one point of the latter is selected, for instance that which gives flexion of the arm, its excitability can be equally modified from several points of the cerebellar cortex. Beck and Bikeles [4, 5] have studied the electrical variations of the cerebellar cortex after stimulation of the cerebral motor cortex. They were not able to detect any local correspondence between the latter and the cerebellum. Miller and Banting [26] have shown that electrical stimulation of a certain point of the anterior lobe inhibits decerebrate rigidity in both homolateral limbs and excites bilateral movements.

These observations, however, cannot be used as objections to the system of localization which has been developed in the above pages. The conception of the cerebellum as an organ for the reflex adjustment of static and dynamic equilibrium involves necessarily the idea of a widespread representation in the cerebellar cortex of almost all motor activities. All movements, even of the most peripheral parts of the extremities, imply activities of fixation of the trunk musculature and the joints proximal to that which is interested in the action. Noica [27] has demonstrated how cerebellar disturbances diminish or disappear in the extremities if the proximal joints are fixed passively during the movements.

It is therefore not surprising to find that cerebellar lesions generally produce widespread symptoms. But especially we have to expect the most severe symptoms in lesions of the anterior and posterior lobes. My own experiments showed that lesions of these parts really result in severe disturbances. Simonelli [34] states the removal of the posterior lobe produces a very grave disturbance of all the motor functions of the animal. The experiments of Weed, and of Banting and Milner [26], according to which electrical stimulation of the anterior lobe elicits manifestations in the whole body, inhibition of the decerebrate rigidity &c., are also in accordance with this.

The above pages have been mainly concerned with the knowledge of the anatomy and physiology of the cerebellum acquired from studies on animals.

Hitherto the endeavour to apply knowledge acquired by experimental studies in animals to clinical phenomena have not been quite successful. It must be here emphasized that the human cerebellum is built according to the same principles as the mammalian cerebellum.

In the highest mammals (the anthropoids) and in man the lobuli ansiformes and paramediani develop into the huge hemispheres that are so characteristic of the cerebellum in these species. There is, according to my anatomical studies, no reason to suppose there exists in the human cerebellum any specific new parts, such as would make it different from others; the part that seems to have especially developed in it is the biventral lobe. This may be related to the specific demands that the erect gait places upon the motor functions of the lower extremities. Accordingly, we should expect to find here the specific leg centre; this assumption agrees entirely with the observations made in the first case described below.

Another conspicuous difference between the cerebellum of man and that of other mammals is that the paraflocculus—the large formation found laterally in all mammals—has undergone regression in man and exists only as the tiny accessory flocculus (Henle). This may be related to the fact that, owing to the erect gait, the trigeminal region has not the same importance in motility in man as it has in quadrupeds, where it is a very important organ for grasping, defence, &c. But, for the rest, there is a complete homology between the lobi ansiformis and paramedianus in mammals and those parts in the human cerebellum extending from and including the lobulus semilunaris superior, to and including the tonsils.

Accordingly anatomical facts indicate that the function of, and localization in, the human cerebellum must be organized in the same way as in the mammalian cerebellum. If the knowledge of the cerebellum acquired from experimental physiology is applied to the clinical symptomatology of cerebellar diseases we immediately will find interesting agreements.

We have above pointed out that the fact that direct vestibular fibres and all the spino-cerebellar fibres run only to the anterior and posterior lobes, indicates that these parts are functionally related to the whole body. This is in accordance with clinical observations. The anterior and posterior lobes form the palæocerebellum, and of this the vermis

constitutes a large part. There seems to be a general agreement that lesions of these parts produce symptoms affecting the whole body, mainly disturbances of the equilibrium, a staggering gait and falling. This is not in contradiction with the assumption of a special centre in the cerebellar cortex for the leg, as will be shown later. If it is the function of the basal parts of the cerebellum to regulate the equilibrium of the body, they must, of course, especially in man and the anthropoids, influence the motor activities of the lower extremities. Hence the principal effect of disease of the palæocerebellum in man is disturbances in the legs (staggering gait, &c.).

A tendency to falling in vermis lesions is often mentioned in the clinical literature; Nothnagel refers to it and states that it usually occurs in a forward or backward direction. Adler [1], Bruns [8], Stewart and Holmes [35], have reported several cases. According to some authors, a lesion in the posterior part of the cerebellum produces falling backwards, and a lesion in the anterior portion falling forwards (Holmes [14]), but on the whole it must be said that there is no general agreement about the direction of the falling. When the lateral parts of the cerebellum are affected the patient falls sideways, either to the same side or to the opposite. The clinical literature thus affords strong evidence that a lesion of the vermis produces falling in a more or less sagittal direction, whereas a lesion of the hemispheres causes falling in a lateral direction. So far, clinical observations are in accordance with the principles of localization that have been discussed in this article.

It must be said that human pathology has offered only slight evidence of a functional localization within the middle lobe. Nevertheless there are a few clinical observations that strongly speak in its favour and tend to corroborate Bolk's conclusions on the localization of function in the most recent parts of the cerebellar hemisphere, which correspond to the mammalian lobulus ansiformis. André Thomas states that the centres of the arm and leg in the human cerebellum are arranged in the same manner as in cats and dogs, the anterior part of lobulus ansiformis being related to the arm and the posterior to the leg. That the arm is related to the anterior part of lobus ansiformis is shown by a case of cerebellar abscess described by Thomas, in which the symptoms were limited to the right arm, though the serious condition of the patient did not permit a careful examination. After death an abscess was found in the substance of the right superior semilunar lobe, but the whole hemisphere seems to have suffered, since it was œdematous and more

voluminous than the left. The fact that the symptoms affected principally the arm gives a certain importance to this case. It speaks in favour of an arm centre in the lobus semilunaris superior.

In his recent publication [36] Thomas gives several instances of cerebellar lesions where the symptoms appeared mainly in the upper or the lower limb. Such observations indicate that there must be a strict localization of these regions of the body in the cerebellum. Unfortunately, the author had no opportunity of correlating his clinical observations with the anatomical lesions and these cases have, therefore, only a restricted importance.

Rothmann mentions a case in which he was able to diagnose an otogenic cerebellar abscess in "the posterior part of the hemisphere," owing to the fact that the ataxia had started in the leg. Marburg finds that tumours of the ponto-cerebellar angle produce more marked symptoms in the arm than in the leg. The first observation of cerebellar disturbances limited to the leg, in which clinical observation had been strictly confirmed by the autopsy, was my first case described in the following pages. It was first published in 1919 [20] and is strongly in favour of this physiological system of localization in the human cerebellum.

Léri [23] published a very important observation in 1917. A soldier, aged 31, was wounded in the neck by a bullet which had penetrated from behind and was found under the occipital protuberance in a relatively superficial position, from which it was easily extracted. There were two wounds, one corresponding to the upper or middle part of the inferior vermis, the other to the left hemisphere. From the rapid regression of the symptoms the author concluded there was a superficial lesion of the cerebellum. Two or three months after the injury this patient had obvious symptoms of cerebellar deficiency, *but in the legs only;* the arms were unaffected. On changing the position of the head in an antero-posterior plane only, the patient developed vertigo. The trembling of the legs also appeared only in an antero-posterior direction. The author draws the following very important conclusions: "There is in man in the inferior vermis a centre in charge of the co-ordination of the motility of the legs. An even superficial lesion here gives symptoms exclusively localized in the inferior extremities (*para-syndrome cérébellaire*)." Furthermore, the author concludes that there must be definite relation between each semicircular canal and special cortical areas in cerebellum from the fact that the vertigo in his case could be elicited only by movements of the head in an antero-posterior direction.

The value of this case is limited by the fact that the site of the lesion was not verified. It is, of course, impossible to form any exact idea of its real extent, but in view of the symptoms I am inclined to locate it somewhat more caudally than the author does. Anyhow, the inferior surface of the cerebellum was certainly injured.

In other respects also this case is exceedingly interesting. Thus the tremor in the antero-posterior plane, and the fact that vertigo was produced by movements of the head in this plane only, agree in a remarkable way with conceptions developed in this article (compare p. 310) .They will later be discussed.

Gordon Holmes [14] writes (p. 115) : " My observations do not lend support to the theory of circumscribed functional representation of different parts of the body in the lateral lobes." A small lesion, according to this author, usually produces symptoms equally from the arm and the leg. But further the author writes : " In a certain number of cases, however, the one limb seemed to be relatively more affected than the other, the leg being more involved by caudal and mesial lesions and the arm by the more anterior. It is possible, then, that there is a " prevalence of representation " in the Rossi sense, the arm being represented more anteriorly and the leg more posteriorly, but this localization is so indefinite that I would not regard it as a trustworthy guide in the diagnosis of a small lesion, such as a cortical tumour."

The evidence reported by Holmes [14], which has been mentioned above, is entirely in favour of the theory of localization that has been adopted in my first cerebellar study in 1918.

Here follows a description of my own two clinical observations, which seem to support the idea that the cerebellar centres in man are arranged in a manner analogous to that found in mammals.

Case 1.—K. G. B., janitor, aged 51 years. Clinical diagnosis : tumour of biventral lobule of the cerebellum ; metastasis from a rectal carcinoma.

Admitted to the medical clinic on August 24, 1918; died September 29, 1918. The patient enjoyed good health until the beginning of 1918, when trouble with defæcation, tenesmus and diarrhœa appeared. He remained at work until the end of July, but had lost about 25 kg. during the year. In August he developed severe headache, referred to the neck, and vomiting.

The patient was received into the Lund University surgical clinic (Professor Borelius) on August 15. In this clinic a rectal cancer was found which could not be operated upon owing to its high position in the pelvis. Ophthalmoscopy on August 12 (Dr. Franck) showed the fundus normal. The persistent severe headache and vomiting made a metastasis in the central nervous system very

probable, and the patient was therefore referred to the medical clinic for a neurological examination.

Abstract from the records in the medical clinic : The patient complains of severe headache, especially in the region of the neck. He is somewhat dull and slow, but answers correctly. On moving in bed he has paroxysms of vomiting and vertigo, especially on turning his eyes towards the right. He usually lies motionless in the bed, with his head turned to the right.

The right plantar reflex was extensor (Babinski), the left flexor, but no other abnormal signs were found except these referable to disturbance of the functions of the cerebellum. It must be especially emphasized that there was no sign of paresis in the right leg. The Achilles and patellar tendon reflexes were normal on both sides. No clonus was present. Romberg's sign was positive, but there was no tendency to fall in any constant direction. There was horizontal nystagmus, with its rapid phase towards the right, and slight adiadokokinesis in the pronation-supination test in the right arm, but none in left. The finger-nose test is carried out promptly on both sides. The knee-heel test is accurate on the left side but much disturbed on the right, the patient throws the right heel roughly and clumsily beyond the left patella up to about the middle of the left thigh, and in moving the right foot back to a spot marked by the examiner's finger on the lower part of the left leg the spot is also passed, though not so far. With the right leg this test is always repeated with the same inaccuracy. This is the more remarkable as the finger-nose tests with both arms, and the knee-heel test with the left leg, are performed with normal precision.

No spontaneous past-pointing from the shoulder-joints either in the vertical or horizontal plane. He also points correctly with the left leg from the hip-joint, but when lying on his back there is considerable past-pointing inwards (medialwards) with the right leg.

Syringing the right ear with cold water produces nystagmus towards the left and past-pointing to the right of both arms from the shoulder-joints, and of the left leg. The right leg deviates towards the left. No tendency to falling is evoked. Syringing of the left ear produces reinforcement of the nystagmus towards the right, past-pointing of the left arm towards the left, and of the right arm to the right, past-pointing in the left leg, wide deviation of the right leg towards the left, and falling towards the left.

Intense vomiting occurred after syringing.

August 27.—To-day the patient falls spontaneously backwards and to the right. Only slight adiadokokinesis in the right arm, none in the left. Finger-nose test prompt and accurate on both sides. The knee-heel test is performed with the same apparent excess of motor innervation as before, the right foot being thrown far above the left knee. With the left foot the movement is performed normally. No paresis of the musculature in the right leg. When told to raise himself from supine into the sitting position with the arms crossed on the chest he fails to sit up because the feet, and especially the right leg, rise from the bed. When in the standing position he attempts to put the point

of the foot upon spots marked by chalk on the floor, the right foot is always moved in a clumsy way far past the mark, even when the patient controls the movement with his eyes. This is more striking when he has to move the foot backwards. Spontaneous pointing unchanged; after rotation to the right on a chair (ten turns in twenty seconds according to Bárány's method) a strong tendency to fall towards the right, with past-pointing to the right in both arms and in the left leg (hip-joint), but none in the right leg. After rotation to the left, past-pointing in both legs and in the left arm, but none in the right arm. After rotation with his head flexed toward the right or left shoulder alternately, the patient can be made to fall backwards or forwards.

During the first week in the medical ward the functions of the cerebellum were examined daily. He was, however, very much troubled by examination and began to vomit intensely as soon as he had to change his position or move himself in any way. Moveover, he suffered much with headache, and during the first week became dull. This of course had an unfavourable effect on the results of the examinations, especially on the testing of the vestibular functions (caloric and rotation tests), but it was possible to carry out without discomfort to him the tests for adiadokokinesis, and the finger-nose and knee-heel tests. Spontaneous pointing from both shoulder-joints remained normal; there was only a slight adiadokokinesis in the right arm; the finger-nose test was performed promptly with both arms, and the knee-heel test with the left. There was a constant deviation inwards of the right leg in pointing while he lay supine, and the spontaneous movements of this extremity were always irregular and clumsy, especially in the knee-heel test. These disturbances were considered to be of cerebellar origin. The general condition of the patient became gradually worse; the somnolence and dullness increased gradually and he died on September 29.

Owing to the cerebral symptoms a cranial tumour was suspected, probably a metastasis from the rectal neoplasm. Since the clinical disturbances were mainly of cerebellar nature this tumour was localized in the cerebellum, and as the symptoms affected the right leg only the tumour was placed in the leg centre of the right cerebellar hemisphere. The existence of a leg-centre in the human cerebellum has never been demonstrated, but from analogy with the mammalian cerebellum I assumed that it lay in the lobulus biventer.

The autopsy made by Dr. J. Fex completely verified the diagnosis. In the right biventral lobe a tumour was found, which on the microscopical examination turned out to be a metastasis of the rectal cancer. (Figs. 3A and 3B).

The cerebrum was free from pathological changes. The cerebellum was normal in shape, but the right hemisphere was somewhat more voluminous than the left. The architecture of the fissures and lamellæ was everywhere

normal, except in the biventral lobe on the inferior surface of the right hemisphere, where the tissue was firmer to the palpating finger. Over a certain area the cerebellar surface was replaced by a greyish-looking firm mass around which the lamellæ curved as if they were pressed apart. In frontal sections it was seen that this was part of the tumour. Its greatest horizontal diameter was 5 cm. and vertical 4 cm. It lay entirely within the lobulus

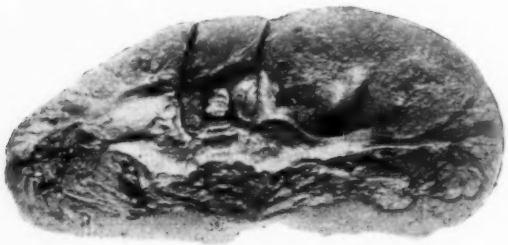

FIG. 3A.—Transverse section through the cerebellum of Case 1. The tumour is seen in its subcortical position on the right side. The white substance and the nucleus dentatus are compressed but otherwise undamaged.

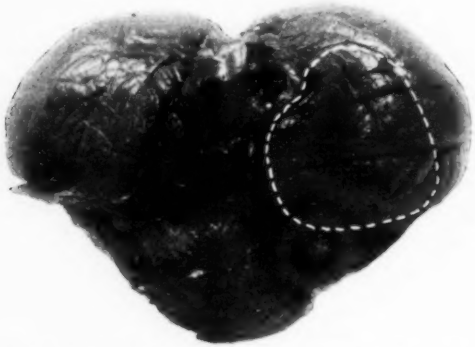

FIG. 3B.—Cerebellum of Case 1. The area surrounded by the white broken line indicates the site and size of the tumour.

biventer, if the lobulus gracilis is considered apart from this. It occupied the whole medial mass of this lobule on the inferior surface of the hemisphere, and was only covered by a thin layer of cortex until the fossa transversa (Ziehen) and flocculus were reached. It was sharply limited by the deep fissure that separates the lobulus gracilis from the lobulus biventer, and spread from here laterally and backwards in the substance of lobulus biventer to the region where the lower anterior surface of the hemisphere borders on the lower posterior surface.

The lower peripheral branches only of the central white substance were involved by the tumour; the main mass was free, but was displaced upwards and backwards. The dentate nucleus also escaped, but its central foldings were pressed somewhat dorsally, and its hilus was compressed.

No other tumours were detected in the cerebellum. The medulla oblongata was a little dislocated towards the left side in the vicinity of the tumour, and was somewhat compressed on its right side. Microscopical examination of the tumour showed it to be a soft carcinoma with a tendency to central necrosis.

The fact that the Babinski sign was positive on the right side is naturally explained by the pressure exerted by the tumour on the pyramidal tract. The section clearly revealed that such a pressure had occurred. The absence of all other signs of a pyramidal lesion makes it impossible to ascribe the motor disturbances of the right leg to the slight impairment of the pyramidal tract, of which the right extensor response was an indication.

Summary.—In this case of cerebellar tumour the clinical symptoms were limited to the right leg, apart from slight adiadokokinesis in the right arm. At the autopsy a tumour was found in the right lobulus biventer of the cerebellum.

There are many arguments, anatomical and others, which strongly support the view that this lobe is related to the functions of the leg. This is the first described human case that in a clear and convincing way shows that the leg-centre is situated in the posterior part of the cerebellar hemisphere, in a position homologous to that which it occupies in the mammalian cerebellum. The site of the tumour was an extremely favourable one, since it occupied the entire posterior region of the lobus posterior (mihi) and this region only.

Case II.—E. M., girl, aged 16 years. Clinical diagnosis: Cerebellar tumour. Pathological diagnosis: Sarcoma of the meninges with extensive growth over the surface of the brain and spinal cord.

The patient's illness began with severe headache and vomiting in the beginning of 1921. After some months a staggering gait developed. In consequence of the severe headache, which was mostly localized in the neck, the patient was received into the University Clinic for Internal Medicine on September 21, 1921. She then had nystagmus, mainly horizontal, of a vestibular type; the right pupil was smaller than the left, and flexion of the head forwards was painful, but flexion backwards not so. Romberg's sign was positive. Gait, even with the eyes open, was very uncertain; she staggered equally to the right and left. The finger-finger, finger-nose and knee-heel tests were performed accurately on both sides. There was no adiadokokinesis. In the right arm there was spontaneous lateral past-pointing from the shoulder-joint, but no error in the left arm. Ophthalmoscopical examination

(Professor Ahlström) revealed choked discs with a swelling of more than seven diopters in both eyes. Vision was seriously impaired.

November 1: Otological examination (Docent Törne): Drums of both ears normal. Hears whispering with both ears at 4 metres. Spontaneous horizontal nystagmus to both sides. Reactions to the caloric test (cold water) perfectly normal on both sides.

November 8: Constant spontaneous past-pointing towards the right with the right arm. Tendency to fall to the right.

November 11: Finger-nose test normal. Romberg's sign negative. Gait normal with the eyes open, but when they are closed the patient deviates towards the right in walking.

November 12: The nystagmus disappears when she turns the eyes to either side for a time. She performs rapid alternate movements well, but somewhat better with the left hand than with the right.

In consequence of the disturbed vision the patient was referred to the surgical clinic, where a trepanation was performed by Professor Gustaf Petrén on November 14.

Abstract from the record of operation.—After opening the posterior fossa on the right side and incising the dura, the cerebellum was found to be under high pressure. Some suspicious looking substance was removed with a sharp spoon from the lateral part of the opening. Punctures were made in two spots of the cerebellar hemisphere to a depth of 3 to 4 cm., but nothing was found, and no tumour was palpable to the finger. As the cerebellum was pressed out of the opening its margins were lacerated. The skin-flap was replaced and the wound sutured; considerable pressure was thereby exerted on the protruding cerebellar hemisphere. The patient was in good condition after the operation.

A microscopical examination of the tissue excised was made at the Pathological Institute by Professor Sjövall: "No signs of tumour or tuberculosis, but in certain regions of the mass there were hæmorrhages, some of long standing. These indicate with certainty an underlying process with secondary toxic or circulatory disturbances in the surrounding substance."

For some time after the operation the patient had intense cerebellar ataxia with typical cerebellar speech. The right eye was deviated to the right, but the other movements of the eyes were normal. There was marked nystagmus to both sides. The right facial nerve was paretic. She heard whispering with each ear at three metres. No paresis of extremities or trunk, and sensibility was everywhere normal. Movements of the right arm were very irregular, slinging and unbalanced. In the finger-nose test the right hand was thrown with force past the nose, or against the forehead, but in this test the left arm was normal. The inferior extremities also showed the same disturbance in movement, the knee-heel test being badly performed on both sides, especially on the right. The patient was unable to sit up in bed without shaking.

This severe general ataxia was the most prominent feature after the operation. After being treated with Röntgen-rays she was then sent home on

February 19. Her condition had at this time slowly improved, so that she could walk, but her gait had the characteristics of cerebellar ataxia.

While at home the patient improved considerably, she had only moderate headache, and no vomiting or vertigo. Her vision improved too. She was able to walk alone and said she did not stagger. She was received into the hospital again on March 3 in order to continue the X-ray treatment.

On her arrival she had a hernia the size of an orange at the site of the trepanation. She is intelligent and bright. She could count fingers at one to one and a half metres with either eye, but her discs were atrophic. There was marked nystagmus, especially in looking to the right. There was no paresis, and the plantar reflexes were normal.

The finger-nose test with the right arm was uncertain, the hand developing a slight tremor at its goal. There was also adiadokokinesis of the right arm and in the left to a less extent. The knee-heel tests were normal on both sides. Romberg's sign was not present but gait with open eyes was staggering and uncertain, the patient sometimes tumbling to the right. Both arms deviated to the right in the past-pointing test in the horizontal plane, but there was no deviation in the vertical plane.

April 4.—Syringing the right ear with cold water produced brisk nystagmus when the eyes were turned to the left, none when they were turned to the right; exaggeration of the past-pointing to the right, and the patient fell to the right. On turning the head to the right the patient fell backwards, on turning it to the left, forwards.

April 8.—Marked nystagmus to the right, none to the left. The finger-nose test shows typical ataxia of the right hand, none in the left.

The patient was again sent home on April 21, after she had three further applications of X-rays. She remained at home till May 18 when she was again admitted to hospital. She had had some headache while at home. Her gait was normal, though she sometimes tumbled to the right; she had fallen only once, when she tried to run. She had nystagmus on turning her eyes to either side, more marked to the right. Sensibility was everywhere normal, and no paresis was detected. Romberg's sign was absent. The finger-nose test showed a slight uncertainty in the right hand, but none in the left, and there was marked adiadokokinesis in the right arm. The knee-heel test was carried out promptly, but there was a slight uncertainty in the movements of the right leg. Gait was staggering and uncertain, and became only slightly more so when the patient closed her eyes.

May 29.—No past-pointing with the left arm, but the right deviated towards the right.

May 30.—The finger-nose test was normal with the left arm, and only slight disturbances in the last phase of the movement in the right. There was marked adiadokokinesis in the right arm, and slighter in the left. On closing her eyes when her feet were together the patient stumbled but did not fall. She walked with her feet widely separated and stumbled slightly.

June 2.—Gait almost normal.

The patient left the hospital on June 22. She was admitted again on August 28 with severe headaches and a large hernia at the site of the operation. She was unable to turn her eyes to the right, and had paresis of the right facial nerve. There was adiadokokinesis on both sides, especially on the right. The finger-nose test was carried out poorly with the right arm, the finger hitting the nose or its vicinity with great force. The knee-heel test was also uncertain on the right side. The arms deviated in various directions in testing for past-pointing owing to the disturbances of movement.

The patient later developed a slight hemiparesis on the right side of the body, became unable to stand or walk, and died on October 2.

An autopsy was performed October 2, 1922 (Professor Sjövall, Dr. Olinder).

A meningeal tumour was found in the right side of the posterior fossa; it also spread widely over the meninges of cerebrum, cerebellum and the spinal cord. It formed a thick layer around the spinal cord throughout its whole length.

The cerebellum, after fixation in formol, was carefully cut in frontal sections. It was then found that the entire left hemisphere was normal and that the vermis had retained its structure, although infiltrated by the tumour, especially in the uvula and nodulus. This infiltration increased on the right side of the vermis, but the right tonsil and a small part of the digastric lobe in the neighbourhood of the tonsil, corresponding to its medial and lower anterior parts, were comparatively well preserved. No trace of cerebellar structure could be recognized in the rest of the digastric lobe. The semilunar lobes had disappeared and the destruction extended into the right part of the lobulus simplex and into the posterior part of the right side of the lobus anterior.

There was a softening of the central white substance below the cortical destruction. No trace of the dentate nucleus could be seen and no normal tissue was found above the level of the peduncles. The nuclei tecti were intact.

Microscopical examination showed that the growth was a meningeal sarcoma.

Summary.—The patient was a girl who, owing to signs of increased intracranial pressure (choked discs with impaired vision), was trephined over the right cerebellar hemisphere, and part of the lateral portion of the cerebellum was removed. After the operation she developed a severe generalized ataxia, undoubtedly due to the intense pressure and tension on the whole cerebellum. The ataxia diminished gradually, and undoubtedly as a consequence of X-ray treatment the general condition of the patient improved in a remarkable way. For a long period she presented no other neurological symptom than signs of cerebellar disturbances in the right arm. Her gait was almost normal, Romberg's sign was absent and the knee-heel test was well performed with the right leg; but there was ataxia in the finger-nose test and

adiadokokinesis of the right arm. Towards the end of her life the most prominent feature was again a general ataxia of the whole body, and hemiparesis. This was undoubtedly caused by the tumour masses found at the autopsy.

The period of temporary recovery was that of greatest interest in this case. We know that such tumours can be influenced by X-rays, and we may therefore assume a regression of the tumour mass leading to the regression of the symptoms. That being so, it is remarkable that during the whole time there was a profound ataxia of the right arm.

A portion of the lateral part of the anterior semilunar lobe had been removed at the operation, and the cortex round the margins of the opening of the skull was lacerated. Later the skin-flap compressed the protruding hemisphere. From earlier cases treated in the same way and studied especially with regard to disturbances of speech, I know that such an operation means a considerable destruction of the cerebellar substance that protrudes into the opening. Undoubtedly the entire cortex of this part of the cerebellum must have been destroyed, directly or indirectly, by the operation. The autopsy verified this assumption.

The anatomical examination in fact showed that both semilunar lobes, the lobulus gracilis, and the rostral parts of lobulus biventer were destroyed. The extensive softening of the central white matter of the right hemisphere is here left out of account, because it had all the characteristics of an acute process which occurred shortly before death. The symptoms exhibited by the patient during her last few weeks have no interest for the questions discussed in this paper.

For a time after the operation there was an intense general cerebellar ataxia in both sides of the body. This may be regarded as an ordinary result of such operations on the posterior fossa. This ataxia diminished gradually, but for several months there was ataxia of the right arm, whereas the cerebellar disturbances of the right leg were only slight. The discrepancy between the symptoms of cerebellar deficiency in the arm and the leg is the most interesting feature of this case. How is it to be explained? According to the theories developed above, the centre of the arm is located in the upper semilunar lobe, whereas the leg-centre is situated in the lobulus biventer and the tonsil. In this case the semilunar lobes were entirely removed, and the remaining parts of the biventral lobe and the tonsil were sufficient to regulate the motor functions of the leg.

Thus the symptoms of this case also are in favour of the hypothesis that the arm-centre of the human cerebellum is situated rostrally to the leg centre. This case, therefore, forms a natural complement to the first case described.

Bárány [3] has studied the clinical symptoms of vestibular lesions in an ingenious manner, and has been led by this work to a conception of another system of cerebellar localization. According to him the vestibular reactions (past-pointing, tendency to fall) produced by irritation of the vestibular apparatus, are elicited by way of the cerebellar cortex. The works of the Dutch physiologists, Magnus and de Kleijn, however, disprove this hypothesis upon which his whole system of localization is based. They have found that the ordinary reactions of the extremities and trunk evoked by irritation of the vestibular apparatus are not in any way influenced by total ablation of the cerebellum. They have thus conclusively shown that the reflex mechanism of the vestibular reactions is not related to the cerebellum.

On the other hand, Bárány has conclusively shown that reactions similar to those appearing after vestibular lesions may be elicited from the cerebellum. Thus he has found that after cortical lesions of the cerebellum typical deviations of the limbs occur (past-pointing in different directions). Bárány's results have been corroborated by several authors, as Holmgren, Berggren, Boivie, Schmiegelow and others. Trendelenburg's method of cooling the cerebellar cortex has proved to be a useful mode of investigation. By cooling different areas of the cerebellar cortex Bárány has been able to produce deviations in different directions in the past-pointing tests.

Bárány believes that the main principles of cerebellar localization is a representation of the different directions of movement at the joints. As each joint can be moved in four directions, upwards and downwards, medially and laterally, it must be represented in the cerebellar cortex by four tonus centres, one for each direction of movement. If one centre is paralysed by a lesion or by cooling, the antagonistic centre prevails, and the result is a deviation in the direction of the action of this antagonistic centre. Thus, if the inward centre for the arm is disturbed, the arm deviates laterally in the pointing test. Bárány has lately reviewed this theory [3].

The situation of the tonus centre for inward deviation of the arm seems to be well established; paralysis of it produces past-pointing of the arm. This can be easily induced by cooling the cerebellar cortex

with ethyl chloride in persons in whom the mastoid process has been removed, so that the dura lies directly under the skin ; this produces deviation outwards of the homolateral arm. Bárány says that he has been able to perform this experiment at least forty times with the same result, and he therefore considers this centre is definitely established.

Gordon Holmes, who has made an extensive study of injuries of the cerebellum during the war [13], concludes his studies of the pointing reaction by stating that in almost all his cases there was a tendency to past-pointing outwards, wherever the lesion was situated in the cortex. This is a strong objection to the supposition of a special tonus centre for inward deviation.

The present writer [21] has recently found that past-pointing can be induced from a purely spinal mechanism. If a person stands with his feet close together and points towards a given point, his finger will deviate laterally if during the test the other arm is abducted. This lateral past-pointing depends only on the disturbance of the static conditions of the body produced by the abduction of the other arm. I have called this phenomenon *spinal past-pointing*.

Thus a disturbance of the static conditions of the body gives rise to past-pointing. From experimental investigations we know that a lesion of the cerebellum produces disturbances of muscular tone, that is, static disturbance of different parts of the body, and it seems to me that the only one of Bárány's observations that has been definitely established, namely, the past-pointing outwards, may be explained as a secondary phenomenon produced by a general disturbance of static conditions following any lesion of the cerebellum.

Bárány has described a tonus centre for downward deviation in the medial part of lobulus semilunaris inferior, close to the vermis. Destruction of this centre should give rise to past-pointing upwards of the arm. One of my patients in whom there was a solitary tubercle situated exactly in this region, nevertheless pointed downwards before the operation [18]. The tumour was successfully removed by Professor Borelius. On the excised piece of the cerebellar cortex it was easy to recognize that the tissue removed was the medial part of lobulus semilunaris inferior. After the operation there was no deviation. This, which must in all respects be considered a pure case, strongly contradicts Bárány's hypothesis of a tonus centre for downward deviation in this region ; Bárány himself [3] admits that it is a serious objection to his hypothesis.

According to Bárány the centre of the leg and arm are situated

together in lobulus biventer. He denies that the arm and the leg are represented in a manner analogous to that determined by experiments on animals. That past-pointing is produced from the same region of the cerebellum in either the leg or in the arm can be, it seems to me, explained by the fact that any lesion of the cerebellum brings about a disturbance of static conditions of the body, and that this results in past-pointing of different parts of the body.

Conclusions.

The basal portions of the cerebellum, situated immediately above the fourth ventricle, are phylogenetically the oldest parts of the cerebellar cortex. Special attention must in future studies be paid to these parts, which have hitherto been neglected. Anatomical facts indicate that they are endowed with important functions.

The most characteristic feature of these basal regions is that they receive fibres directly from the vestibular nerves, according to studies previously made by the author.

The histological uniformity of the cerebellar cortex, even in the human cerebellum, indicates that function and organization of function are probably essentially the same in the whole organ. All evidence on the function of the basal regions will therefore be of the greatest value for an understanding of that of the whole cerebellum.

After lesions of the basal parts motor phenomena known as " forced movements " occur.

It has been shown by Russell, Ingvar, and Simonelli that these forced movements after lesions of the posterior lobe appear chiefly as a falling backwards. These same authors have demonstrated that the more posteriorly the lesion lies, the more pronounced is this falling backwards during the acute stage.

Since the forced movements resemble strongly those appearing after lesions of the vestibular apparatus, it is logical to regard the forced movements after cerebellar lesions as being due to disturbance of the vestibular innervation of these parts.

Both the vestibular and cerebellar forced movements always take place in a definite plane of space. When such lesions involve the anterior or posterior parts of the basal region the forced movements take place in a sagittal plane around a frontal axis, while lesions of the lateral parts of the cerebellum give rise to forced movements in the frontal plane around a longitudinal axis.

Since those associated with lesions of the anterior and posterior

parts of the vermis resemble those produced by lesions of the vertical semicircular canal, it is logical to conclude that this canal is specially connected with these regions of the cerebellum. Certain clinical observations speak in favour of this hypothesis.

The fact that forced movements disappear soon after the infliction of the lesion is not an argument that they are not of cerebellar origin, or without importance for our knowledge of cerebellar physiology.

As the basal regions of the cerebellar cortex with their intimate vestibular connections are, in the literal sense of the word, a sort of calyx which encloses the major part of the cerebellum, which is developed later in phylogenesis, so the functions of the labyrinth may be considered to include in embryo those of the cerebellum. There is during phylogenetic development a tendency of regression of the vestibular influence on cerebellum, whereas the spinal influence increases (strongly developed spino-cerebellar tracts in higher animals). Morphological and histological studies have provided ample evidence that the cerebellum is an identical organ in all vertebrates. There exists a complete homology between all parts of all cerebellums, except in the case of the bony fishes. Accordingly, in all the same system of functional localization must hold.

A long series of experiments on the cerebellum has shown that in animals the limbs are at least to a considerable extent represented in special regions of the cerebellar cortex (lobulus ansoparamedianus, Bolk), and that the centre of the fore limb is situated rostrally to that of the hind limb.

Two cases are described in this article which strongly support the view that in the human cerebellum there is the same arrangement of the centres of homologous parts.

In the first case, where a tumour lay in the right lobulus biventer, the only clinical symptom was cerebellar ataxia of the right leg. In the second case the right hemisphere was injured extensively by an operation, and post-mortem examination showed that a large part of the hemisphere (semilunar lobes, lobulus gracilis, part of lobus biventer) had been completely destroyed. The severe general ataxia that followed the operation disappeared gradually from all parts of the body except in the right arm, though a slight disturbance of a cerebellar type was also noticed in the right leg.

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THE OCCURRENCE IN OSTEITIS DEFORMANS OF LESIONS OF THE CENTRAL NERVOUS SYSTEM, WITH A REPORT OF FOUR CASES.

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MUCH has been written on osteitis deformans since Paget first gave his classic description of this disease in 1876. It is well known that the nervous system is rarely affected, in spite of the alterations that occur in the bones which surround the brain and spinal cord, as well as in the neural foramina of the skull and vertebral column. The rarity of cases reported in the literature in which neurological signs were present is striking.

The essential changes of the disease consist in a primary absorption and rarefaction of bone, followed by an excessive formation of fibro-osteoid tissue. In this way the consistency of the affected bones becomes softened. These lesions occur most frequently in the bones of the skull, the long bones of the extremities, and very often in the vertebral column.

In the cranium extensive alterations are produced by the abnormal condition of the bones. While the facial bones are not infrequently affected, attention here is chiefly concerned with the osseous structures which envelop the brain. The skull is increased in size. In shape it commonly becomes more square and may show bossing. The latter deformity is seen most frequently upon the vertex. An increase in width is an outstanding feature of the altered shape of the head. In many cases the sides of the skull bulge prominently, so that the ears come to be tilted outwards. Prominence of the frontal region is also frequently present.

The cranial bones are increased in thickness, often to an extreme degree, and the sutures, especially at the vertex, are frequently obliterated. Differentiation into outer, middle and inner tables of a severely affected bone, seen in section, is seldom possible. On the inner aspect of the cranial vault the greatest thickening and irregularity

are commonly seen in the region of the frontal and anterior halves of the parietal bones. In this area flattened exostoses are sometimes present, producing great unevenness of the bony surface. The occipital bone, though participating in the general increase in thickness, usually has a less irregular surface. The bones at the base likewise become thickened.

The sella turcica in a few cases has been found altered in shape, the alteration consisting in a flattening out of the fossa, but in a series of six skulls Hurwitz found the sella turcica altered in one only. Léri and Jefferson both mention cases in which the fossa had become very shallow. In Jefferson's case, which was examined radiographically, the sphenoidal sinus appeared very large. On the other hand this sinus may be greatly reduced in size; I have recently had the opportunity of examining a skull, severely affected by osteitis deformans, in which it was filled in by bony overgrowth.

The internal configuration of the skull is markedly altered. As mentioned before, an increase in its breadth is an almost constant feature. This widening is not only accounted for by the greater thickness of the bones, but also by an actual increase in the transverse diameter of the interior. The antero-posterior diameter is lengthened, but to a less extent. The vertical measurements of the cavity, however, are decreased, especially in the region of the foramen magnum, as has been pointed out by Léri.

That portion of the base surrounding the foramen magnum which is supported by the spinal column is maintained in position, while the various cranial fossæ tend to sag down around this central point. An important factor in the production of this sagging is the weight of the cerebral hemispheres. The peripheral portions of the lesser wings of the sphenoid and of the petrous temporal bones sink downwards. At the same time the degree of upward slope of the anterior or basilar portion of the occipital bone and of the dorsum sellæ becomes reduced or lowered. In this manner the base of the skull comes to be flattened out to a certain extent. This altered formation has been termed "platybasie" by Léri.

In more extreme cases of sinking of the peripheral portions of the base, the basilar part of the occipital and posterior part of the sphenoid bones may actually have the appearance of having been pushed up into the cranial cavity, producing an elevation. To this deformity Léri gives the name of "convexobasie."

It has long been recognized that the neural and vascular foramina

at the base become reduced in size, though some observers have made a contrary statement. Léri, however, in 1913 drew particular attention to the narrowing of all the basal foramina, including the foramen magnum, in skulls affected by osteitis deformans.

The extent of reduction in the calibre of the individual foramina is commonly unequal, depending upon the degree of abnormality in the bones surrounding them. While the reduction in size of the neural foramina may be accepted as a constant feature, narrowing of the vascular foramina is by no means always present. In the first case described by Paget enlargement of all the channels and apertures for blood-vessels was noted at the autopsy. Humphry reported in one case increase in size of the carotid canal and of the foramina spinosa. It is usually observed that the grooves on the inner surfaces of the bones for the meningeal vessels are much deeper than normal. The pulsatile properties of the vessels may have something to do with this.

The absence of cerebral compression in osteitis deformans of the skull has been accounted for by the intracranial pressure exerting its influence upon the bones in their softened condition, at the time the cranial deformities develop. Consequently, though the various diameters of the cranial cavity may be altered, the capacity of the skull in osteitis deformans has not been found to differ from that of the normal.

On the other hand the freedom from compression of the cranial nerves in almost all cases is more difficult to understand. Two cases will be described later in which, however, both the optic and ocular nerves were involved (Cases 3 and 4).

Osteitis deformans of the vertebræ commonly gives rise to static deformities, such as curvature, rigidity and diminished stature. Hurwitz reports cases in which gradually as much as $7\frac{1}{4}$ to $13\frac{3}{4}$ inches have been lost in height. While in the majority of patients these changes are due to the softened condition of the bones, in some a shrinkage of the fibrous and cartilaginous attachments of the vertebræ has appeared to be the only cause present.

The curvature is usually rounded and very seldom angular. Deviations of a scoliotic nature are relatively infrequent. Cases have been reported in which the spine was straight and yet the vertebræ were extensively affected.

While most of the vertebræ are usually affected to some degree in osteitis deformans of the spine, it is not uncommon to find crushing and obvious deformity limited to a few contiguous vertebræ. Or the body of one vertebra may be much reduced in depth and sometimes displaced.

Lipping of the lateral edges of the bodies is a common deformity; these exostoses sometimes unite over the intervertebral discs. Such bony hyperplasia is often extreme and may produce an appearance as if candle grease had trickled down the sides of the vertebræ. The spinous processes are usually held firmly together by an osteo-fibrotic ankylosis. The intervertebral foramina in those areas of the spine most markedly affected are often considerably reduced in size in an irregular manner; it is, therefore, the more remarkable that radiating pains, such as could be attributed to compression of the dorsal roots, are infrequent.

The possible deformities produced by osteitis deformans of the vertebræ, as they affect the lumen of the spinal canal, have been practically disregarded in the literature of the disease. That the canal may be reduced in size even to the extent of compressing the spinal cord, will be made clear by the descriptions of two of the cases which follow. This complication must be rare, as no reports on similar cases have come to my notice in the literature. I have also been able to prove that reduction of the calibre of the spinal canal and irregularities in its walls may develop in osteitis deformans by the examination of the vertebral column of a cadaver.

The two cases of compression of the spinal cord which occurred in patients suffering from osteitis deformans were admitted to the National Hospital, Queen Square, one under the care of Dr. Gordon Holmes, the other under Dr. Kinnier Wilson, to whom I am indebted for permission to make the following reports.

Case 1.—J. H., aged 55, clerk, was admitted November, 1922. He gave no history of injury. He had been operated upon for rectal fistula when aged 45. He had contracted gonorrhœa twice in youth; his health otherwise had been excellent, and he had led an active life. Both his parents were healthy; he was the only surviving child, one other infant having been born dead. He himself had four healthy children, while two others died in infancy.

In September, 1921, he began to experience a sharp lancinating pain in the buttocks when walking. He also noticed that his feet always felt cold, although previously he had been troubled with hot feet. Shortly afterwards he noticed that the right leg was becoming weak, and later the left leg began to feel stiff. He found he could walk one mile only without the aid of a stick.

Towards the end of 1922 both legs became much weaker, but he could still "shuffle" along with the aid of two sticks. On attempting to walk he had pain like sciatica down the left leg. Six months previous to admission he had noticed, while having a hot bath, that the water felt cold to his feet.

Bladder trouble, in the form of straining and frequency of micturition, had been present for four months. The bowels were constipated and rectal control

was defective after purges. For six weeks before admission he had "muscle spasms" commencing at the knees and spreading up as a tight feeling to the middle of the abdomen. There was no definite girdle sensation. The spine in the lumbar region was tender.

On admission patient was of a stout, plethoric build with a high complexion. His weight was 13 st. 6 lb. The features betrayed no deformity of the facial bones. The skull was large and prominent, and bulged over both ears, with a high boss over the forehead. He stated that "a hollow across the top of the forehead had become replaced by a lump." Two to three years previously he wore size $6\frac{7}{8}$ in hats, but now required $7\frac{1}{2}$ size. The top of his head sometimes ached and felt hot. Only the front lower teeth remained; these were in proper alignment, and did not show signs of "alveolite expulsive," a condition described by Léri in which owing to the maxillæ being affected the dental alveoli became reduced in size and the teeth slowly expelled. His neck was short and thick and his head inclined slightly forwards. In the lower cervical and upper dorsal region the curve of the spine was more rounded than normal. When standing the patient showed a distinct stoop, and had difficulty in raising the head to look upwards. He remarked he was not as tall as he formerly was. The left tibia in its lower third presented a hard and painless fusiform swelling. On passive manipulation there was no limitation of movement at the ankle-joint. There was no external evidence of deformity, other than in those parts of the skeleton already mentioned.

The ocular fundi were normal, no lens opacities were discovered and the visual acuity was unimpaired. The functions of the cranial nerves were unaffected.

No motor or sensory disturbance was present in the upper extremities. On the trunk, below the level of the third costal cartilages and including the lower extremities, there was an impairment of moderate degree to all forms of sensation, and immediately above the upper level of this sensory disturbance a narrow zone of hyperæsthesia. The action of the intercostal and abdominal muscles was poor. Both legs were paretic, the right being weaker than the left. No muscular wasting was observed.

The superficial abdominal reflexes were absent. The plantar responses were extensor in type. The deep reflexes of the lower limbs were exaggerated.

In the cardio-vascular system the radial arteries were moderately thickened and the pulse tension raised. The temporal vessels were tortuous. The cardiac dullness was increased on the left to beyond the nipple line. In the examination of the other systems no abnormality was detected.

Lumbar puncture was unsuccessful. Considerable difficulty was met with in entering the spinal canal, as the needle everywhere encountered bone, the consistency of which was softer than that of the normal. Finally, when the point of the needle penetrated the theca no fluid escaped. The Wassermann reaction of the blood was negative.

On radiographic examination the bones at the vertex of the skull showed

marked thickening and mottling. The outline of the outer table was faint and very hazy in the fronto-parietal region. That of the inner table was more dense but definitely irregular in the same area. The outlines of the occipital bone were smooth but showed a sinking of the occipital fossa in relation to the foramen magnum. At the base the bones gave the appearance of a flattened surface similar to the type of "platybasie" of Léri. In the region of the mastoids the air cells appeared enlarged and the bone rarefied. The sella turcica was unaltered in size, but the sphenoidal sinus appeared larger than normal. The palatal bone appeared to have been tilted slightly downwards and forwards.

A skiagram of the upper dorsal spine indicated the presence of lipping of the edges of the vertebræ. The lower half of the left tibia showed signs of rarefaction with increased thickness of the outer compact layers, especially on their mesial aspect; the bone was bowed forwards, thus increasing the space between the tibia and the fibula.

In this case, because of the slowly progressive character of the patient's disability and the evidence of localized compression of the spinal cord, operative interference was decided upon. On November 28, 1922, Mr. Percy Sargent performed a laminectomy of the second to the fourth dorsal vertebral arches. At the operation the bone was found thickened and softened, cutting easily with the forceps. The perithecal space was absent and the inner surfaces of the laminæ lay in close apposition to the dura mater. Pulsation of the dura was at first very feeble, but improved as the decompression was effected.

A good recovery was made by the patient, and two months later he was discharged able to walk with considerably greater ease than on admission. The sensory disturbances were unchanged in the level to which they had previously attained, but were greatly diminished in degree. Sphincter control was almost completely regained.

A piece of bone removed at operation showed microscopical changes typical of osteitis deformans. Rarefaction was observed and osteoclasts were numerous, in many cases lying against and eroding the bony lamellæ. The latter were very irregular in direction and in places outlined by a row of osteoblasts. A highly cellular fibro-myxomatous looking substance occupied the spaces between the lamellæ.

Case 2.—V. C., aged 63, was admitted March, 1920. His previous health and family history revealed no points of importance. No history of venereal disease was obtained.

When 49 years of age he began to suffer with sciatica of both legs. The neuritic pains were associated with spasms and cramps in both legs, and he had some difficulty in controlling his urine. These symptoms disappeared within a period of two years.

At the age of 61 he underwent an operation for the removal of hæmorrhoids. A short time previous to the operation he had observed that his feet often became numb and blue. Soon after the operation he noticed that his legs were becoming unsteady, and he fell down on several occasions.

Within the space of a year he began to have difficulty in raising his feet off the ground, and the legs felt heavy. He also began to experience a sensation like that of a tight band round the upper part of the abdomen. It was only on being medically examined that he discovered that he had lost sensation in his legs. Subjectively there was some numbness in the feet only. He did not have any pain in the limbs and the spine was not tender. The paralysis of the lower extremities rapidly became complete. Bladder trouble was present in the form of precipitant micturition, and rectal control was defective.

On admission to hospital he was thin, but looked younger than his age. The vertebral column was very rigid and showed a prominence of the ninth dorsal spinous process, but no angulation. The spinal curves were not exaggerated. No other skeletal deformities were noticeable. He usually lay in bed with the legs drawn up and flexed at the knees. The arterial system showed marked tortuosity of the superficial arteries and the vessel walls were thickened.

The cranial nerves were unaffected, the fundi were normal and no signs of cataract were present. Sensory disturbance over the trunk and lower limbs was evidenced by an almost complete loss to tactile, painful and thermal stimuli up to the level of the xiphoid cartilage. The appreciation of vibration was absent below the level of the seventh dorsal spine. In the lower limbs there was a complete loss of the sense of position in space.

Paralysis in flexion was present in the legs. The lower intercostal muscles did not act, and breathing was mainly diaphragmatic. Changes in the tendon reflexes consisted of exaggeration of the ankle-jerks. The knee-jerks, however, were difficult to obtain, owing to the degree of spasticity present. The plantars were extensor in type, and the superficial abdominal reflexes were absent.

By lumbar puncture a very small quantity only of cerebrospinal fluid was obtained, which was yellow and immediately coagulated on standing. The possibility of Froin's loculation syndrome occurring in osteitis deformans of the vertebræ has been mentioned by Greenfield, who cited the above case as an example. In his paper the microscopical appearances of a section of bone from one of the laminæ are shown, and are typical of those present in this disease.

Skiagrams of the upper dorsal region of the spine suggested the presence of a tumour at the level of the fourth and fifth dorsal vertebræ. In this area an irregular swelling appeared to project from the lateral aspect of the spine.

An exploratory laminectomy was performed by Mr. Percy Sargent. No tumour was seen, but the laminal arches were found to be definitely thickened. Pulsation of the cord was not at first apparent, and did not appear until the laminectomy was extended upwards beyond the level of the fourth dorsal laminal arch. At a later date the patient died, and for the following notes on the condition of the spinal column seen at autopsy I am indebted to Dr. J. G. Greenfield: "At the level of decompression the vertebral laminæ looked rather thicker than usual and were softer in cutting. Below this level the thickening and softening of the laminæ became progressively more marked, so that in the

lower dorsal and upper lumbar regions the bone could be picked away by a dissecting forceps. The thickening of the bone caused the spinal canal to be narrowed so that the dura mater was everywhere in contact with the bone. It was also abnormally adherent to the bony arches all the way round. The cord was removed and appeared normal. At the lower part of the body of the eighth dorsal vertebra a small nodule projected backwards from the vertebral body, and a smaller nodule of a similar character was present on the body of the sixth dorsal vertebra. There was a depression of the anterior surface of the spine at the lower end of the tenth dorsal vertebra, as though the eleventh vertebral body had been displaced backwards. The body of this vertebra was reduced in depth. Below this level the contour of the lumbar spine was irregular. There was no evidence of thickening or bossing of the skull."

Both of these cases demonstrate the possibility of compression of the spinal cord as a result of the bony lesions of osteitis deformans affecting the vertebræ. The manner of compression is evident. Firstly, the increased thickness of the softened bones is not only productive of deformities on the external surface of the vertebræ but may also bring about a narrowing of the lumen of the vertebral canal. Secondly, the presence of bony excrescences projecting from the inner surfaces of the bones, as were found at autopsy in the second case, suggests an additional element in the production of compression. Two points in favour of the view that the spinal canal is reduced in size in such cases are afforded by the absence of the perithecal space and of the normal pulsation of the cord.

In both my cases the vertebral column was undoubtedly affected throughout the greater part of its length, but the encroachment on the spinal canal was not uniform, for there were in both cases symptoms attributable to local compression of the spinal cord. In neither case was there any external evidence of gross deformity, such as angulation or marked curvature, and spinal tenderness was absent. In the second case the bony changes typical of osteitis deformans appeared to be limited to the vertebræ.

By the kindness of Sir Arthur Keith, an opportunity was afforded, at the Royal College of Surgeons, of examining the vertebral column of a cadaver, in which the skull, facial bones, spinal column and many other bones of the body were extensively affected by osteitis deformans. Unfortunately with this specimen no clinical history was available.

The spinal column presented a moderate curvature of the dorsal vertebræ, with the convexity directed backwards, the lower dorsal vertebræ being the most prominent. From the second dorsal vertebra downwards a condition of osteo-fibrotic ankylosis of the spinous

processes was present. In a macerated portion of the spine there was some lipping of the lateral edges of the bodies of the eighth, ninth and tenth dorsal vertebræ. Laterally the bodies of the ninth and tenth were almost fused over the intervertebral disc by this process. The intervertebral foramina were very unequal in size and many appeared to have been narrowed.

The spine was cut across at several levels. Alterations in the structure of the bone were most noticeable in the ninth and tenth dorsal vertebræ. The lumen of the spinal canal appeared distinctly small in comparison to the size of the vertebræ, especially in the lower dorsal region, the reduction in the dimensions of the canal being chiefly at the expense of its antero-posterior diameter. This diameter measured 12 mm. at the level of the ninth dorsal verebra. For contrast the antero-posterior diameter of the vertebral foramen was measured in the ninth dorsal vertebra from five normal adult skeletons and found to vary from 15·5 to 18 mm. While the transverse diameter of the canal in the diseased vertebra was 18 mm., this measurement varied from 15 to 18 mm. in the five normal vertebræ examined.

Inspection of the lumen of the canal formed by several normal vertebræ retaining their attachments to one another, showed throughout an evenly smooth surface. In the diseased spine, however, the inner surface both of the bodies and of the laminal arches was decidedly uneven. The greatest encroachment upon the canal was in the region of the laminal arches, due to the bulging inwards of their thickened superior articular processes.

The reduced size of the canal, its irregularity, and the lipping of the edges of the vertebral bodies, are well shown by the accompanying illustrations (figs. 1, 2 and 3).

Among the uncommon cases of osteitis deformans of the vertebræ, in which the presence of lesions of the spinal cord have been discovered, may be mentioned that of Marie and Léri. In this case a syringo-myelic cavity was found to extend from the first cervical to the second dorsal segment of the cord. Subjectively the patient had complained of vertigo, and pains in the back and hips. Sensation, however, was stated by the authors not to have been grossly affected.

Gilles de la Tourette and Marinesco have reported the case of a man of 49, in which the skeletal tissues were widely affected, including the small as well as the large bones. During life the reflexes, the control of the sphincters and sensation were normal. Macroscopic and microscopic examination of the spinal cord revealed the presence of certain

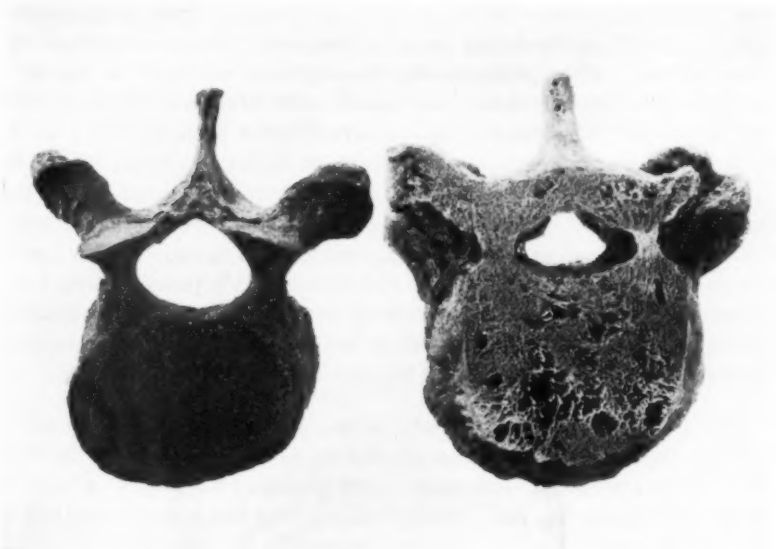

FIG. 2. FIG. 1.

In fig. 1 the lower half of the ninth dorsal vertebra of a case of osteitis deformans is shown. Rarefaction of the body with increase in size of the spaces between the lamellæ is conspicuous. In fig. 2 is seen a normal ninth dorsal vertebra for comparison. The difference in the lumen of the spinal canal of the two vertebræ is very obvious.

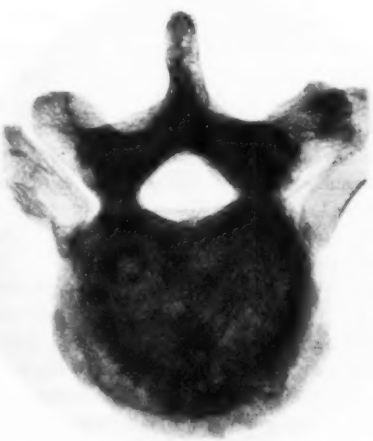

FIG. 3.—Skiagram of bone seen in fig. 1, showing rarefaction.

changes in the posterior columns and in the posterior part of the lateral columns, chiefly in the dorsal region of the cord. The cervical cord was not examined. These changes, slight in degree, consisted of an unevenly distributed rarefaction of the myelinated nerve fibres and of an increase in glial tissue. The anterior and posterior nerve roots appeared to be normal. It was suggested by the authors that the alterations in the bones were possibly of a trophic character, occurring secondarily to the changes in the cord itself, rather than the reverse. Several other cases have been described in which changes were found in the cord similar in nature to those mentioned in the above case. It is possible that such lesions represent the earliest effects of compression, before the gradual narrowing of the vertebral canal is sufficiently advanced to produce clinical signs of compression of the cord.

In the next two cases atrophy of the optic nerves was present in patients in whom the skull was affected by osteitis deformans. In both diplopia also occurred, indicating most probably an injury of one or more of the ocular nerves. Several of the long bones were involved in one of these cases, and the vertebral column in the other.

Case 3.—K. H., female, aged 61, was admitted December, 1922, under the care of Dr. Gordon Holmes. She had undergone an operation for polypus of the uterus at the age of 55. Her health otherwise had always been good, and both her parents had been healthy. She herself was married, but had had no children and no miscarriages.

At the age of 53 diplopia developed suddenly. The resulting visual confusion was sufficient to cause her to fall down on several occasions. Within a period of six months the diplopia disappeared. She had no headaches during that time. When about 55 years of age she began to suffer from "rheumatism or neuritis" in the right upper arm. These pains ceased at the age of 60. At this time, however, she noticed that the right humerus bulged forwards at its upper half. There never was any stiffness or limitation of movement at the shoulder-joint. At the age of 60 the sight of her right eye began to fail. She consulted Mr. Leslie Paton, who discovered signs of atrophy of both optic nerves. During the four months before admission the impairment of vision in the right eye increased rapidly.

The skull was large and appeared swollen and protuberant above the ears on either side. This bulging was more noticeable upon the right than the left side. The shaft of the right humerus was thickened and curved forwards in its upper half. At the right knee-joint the condyles of the femur appeared enlarged and measured more in diameter than those on the left side. She remembered an injury having occurred to the right knee-joint several years previously.

A lateral skiagram of the skull showed diffuse thickening of the frontal

bone and an irregular uneven thickening of the other bones of the vertex. The bones at the base gave the appearance of having been pressed upwards in the region of the base of the sphenoid, conforming to the type of "convexobasie" of Léri. The dimensions of the pituitary fossa appeared to be normal. An antero-posterior skiagram showed well the extent of the bulging in the parieto-temporal regions.

The shaft of the right humerus was thickened and mottled in appearance, especially in its upper half, and there was rarefaction of the bone surrounding the glenoid cavity. Thickening and rarefaction were apparent of the lower end of the right femur, including the condyles.

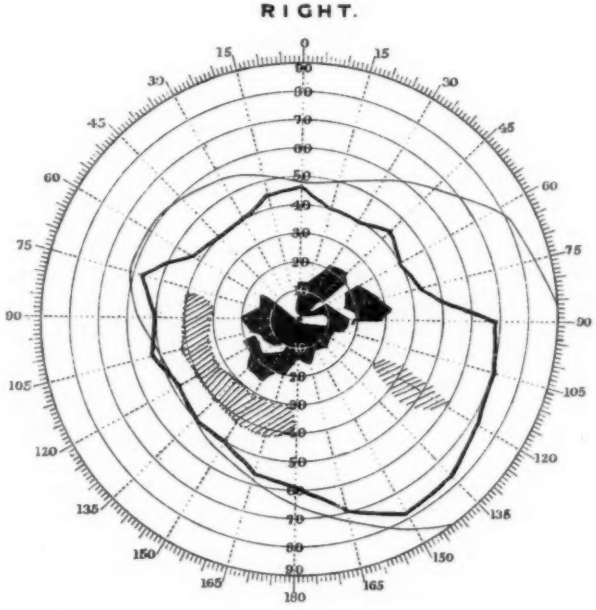

FIG. 4.—Visual field of right eye to a 10-mm. white object, showing central and para-central scotomata. Colour vision retained at fixation point only. Central vision clear, peripheral vision indistinct.

Nervous system.—The visual acuity was $\frac{6}{12}$ in each eye. On ophthalmoscopic inspection the right optic disc was found to be pale all over, with a greater degree of pallor in the temporal than in the nasal half. The lamina cribrosa was visible. In the left disc there was pallor of the temporal half only. The edges of both discs were clear and the vessels of good size.

In the right visual field there was a large irregular scotoma which prac-

tically surrounded the fixation point, and a partial scotoma nearer the periphery in the inferior and nasal areas. Some constriction of the field was present, most marked in the two upper quadrants. The left visual field was full, and no evidence of scotomata was discovered.

The reactions of the pupils were normal. Hearing was considerably impaired in the right ear, conduction by bone being better than by air. In the left ear hearing, as tested by ordinary methods, was not affected. No other abnormalities of the cranial nerves were discovered. The Wassermann reaction of the blood and cerebrospinal fluid was negative, the cytology and protein content of the latter being also normal.

Case 4.—N. N., female, aged 52, was admitted September, 1923, under the care of Dr. Gordon Holmes. She had always been delicate. She had two children living, both in good health, while a third pregnancy had resulted in a "freak."

About four years previous to admission she suddenly developed double vision. This persisted for three months, and since had recurred for short periods. Soon after the onset of diplopia her sight began to fail gradually. Lately the visual impairment progressed more rapidly. She also became increasingly deaf in the last four years. Her height had gradually diminished by as much as 6 inches. It was noticed by her relatives that her head had become larger, and that her features had altered considerably in the last three years. These deformities passed unobserved by the patient until her attention was called to them. She was troubled with pains at the back of the head, and sometimes with a hot feeling over the vertex. For three months before admission she complained of pain at the bottom of the spine, and for some weeks of aching and stiffness of the right side of the jaw.

She was a short flabby looking woman with a slight stoop, and a large broad head sunk upon the shoulders, the chin almost reaching the upper end of the sternum. The lower limbs were separated unnaturally, rotated outwards and slightly bowed below the knee, with the feet turned out. The chest was narrow and the lower costal margins were almost in contact with the iliac crests.

The skull was broad and flat, and bulged at the sides so that the ears were tilted outwards; these were also turned slightly forwards by the enlarged mastoid processes. The back of the head was flattened, while the occipital protuberance was enlarged and lay at a much lower level than normal. The forehead was broad, low and slightly bossed upon the right side. In circumference the skull measured $23\frac{5}{8}$ inches (60 cm.). Both eyes were prominent, the nose sunken and the lower jaw prognathous, giving the features a somewhat froglike expression. Some fulness was present in the region of both temporo-maxillary joints, and the movements of the jaw were restricted and stiff. The gums were edentulous. The hard palate sloped upwards and backwards from its anterior end. There was considerable rigidity of the spine, and the patient had great difficulty in raising the head to look upwards. Beyond some stiffness

at the hip-joints, the movements of the limbs were unrestricted, and no thickening of the long or small bones of the extremities was observed.

A lateral skiagram of the skull showed that the bones of the vault were thickened everywhere, but particularly in the occipital and posterior parietal region. The outline of their external surfaces was vague and extremely irregular, while that of the internal surfaces was more definite. The frontal bone overhung the bones of the face, which were retracted with the exception of the prominent lower jaw. Posteriorly the most dependent part of the occipital bone was at a decidedly lower level than the foramen magnum, and the outline of the occipital fossa was angular in place of being curved. The bones in the region of the foramen magnum had the appearance of having been pressed upwards into the cranial cavity. The pituitary fossa was shallow, and the outline of the clinoid processes very blurred. A skiagram of the lumbar spine showed marked rarefaction of bone. Rarefaction was also observed in the region of the right hip-joint.

Nervous system.—The visual acuity of the right eye was $\frac{6}{24}$, and of the left $\frac{6}{15}$. Inspection of the fundi revealed pallor of the temporal halves of both discs, of slight degree in the right eye, more marked in the left. The edges of the nasal halves of the discs were a little hazy. The calibre of the vessels in both fundi was good, and no retinal changes were observed. No opacity of the lenses was present.

The right visual field showed considerable concentric diminution, while in the left field there was marked restriction of the temporal half, with moderate diminution on the nasal side. No evidence of scotomata, either partial or complete, was discovered. The fields of colour vision were markedly constricted.

The pupils were equal in size, circular, and their reactions brisk. The right external rectus and superior oblique muscles were completely paralysed, but diplopia was not present at the time of examination. Hearing was greatly impaired in both ears, the defect being of the middle-ear type. No other abnormality of the cranial nerves was present and the reflexes, sensory and motor systems, were normal. The mental state of the patient was rather feeble and her memory was much impaired. The Wassermann reaction of the blood was negative.

It appears permissible, by a process of exclusion, to assume that in these two cases of osteitis deformans the atrophy of the optic nerves resulted from their compression within the optic foramina. The state of the pupil reactions and the absence of any clinical sign of tabes dorsalis, in conjunction with the negative result of the Wassermann tests, were evidence against the condition being of luetic origin. The possibility of sinus infection could be set aside by the examination of the skiagrams of the skulls. The clinical histories failed to suggest the existence of any other possible cause of optic atrophy, whether toxic,

infective or familial. Ophthalmologically the cases are of interest, for, as far as can be ascertained, osteitis deformans has not been previously included among the possible causes of optic atrophy.

By permission, an examination was made in the Museum of the Royal College of Surgeons, of two skeletons in which the skulls were affected by this disease. The optic foramina appeared to be reduced in size. In several normal skulls, a probe, roughly 5 mm. in diameter, could be passed with ease through the optic foramina, whereas in one of the affected skulls it became engaged in the walls of both foramina. In the other skull only one foramen could be penetrated by the probe. The capacity of the eye sockets was considerably reduced. This may explain the prominence of the eyes which is present in some cases of Paget's disease of the skull.

Ocular complications, however, are not uncommon in osteitis deformans. Paget himself, after an examination of twenty-three cases, reported that four had become blind; retinal hæmorrhages had occurred in three of these, and choroiditis was the cause of blindness in the fourth. The recurrence of retinal hæmorrhages has since been mentioned by numerous observers. These vascular lesions are more probably due to arterio-sclerosis, which is so commonly present in the subjects of this disease, than to vascular compression.

Coppez has reported four cases in which degenerative changes were present in the retinæ, in the macular and para-macular areas. In none of these cases could syphilis be held responsible for the disease in the fundi. Three cases described by Vergne all showed well-marked choroido-retinitis. In a case reported by Watson "high myopia with a large posterior staphyloma and extensive choroidal changes in each eye" were present. Numerous authors, such as Hurwitz, Vergne, Coppez and Vincent, have noted the presence of crystalline opacities in the lenses.

Paresis of ocular muscles has occasionally been observed in osteitis deformans of the skull. Diplopia developed in one of the cases described by Coppez, and had been present temporarily in the last two cases reported in this paper.

Deafness as a complication of this disease is fairly common. This may be due to compression of the auditory nerve, or, as was more probable in Case 4, to alterations in the bones, leading to disturbances in the sound-conducting apparatus.

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Notices of Recent Publications.

Lehrbuch der Nervenkrankheiten. Von H. Oppenheim. 7te wesentlich vermehrte und verbesserte Auflage. Zweiter Band. S.1389, mit 275 Abbildungen im Text und 9 Tafeln. Berlin: S. Karger. 1923.

The first volume of the new edition of Oppenheim's textbook on nervous diseases, which is now edited by Cassirer, Goldstein, Nonne and Pfeifer, was noticed in a recent number of this Journal. The second volume, which has recently appeared, has received even more additions, and though Oppenheim's original plan has been, wherever it was possible to do so, adhered to, there are many changes, and all of them, as far as can be seen on looking through the book, tend to improvement and completeness. There is a new section devoted to diseases of the basal ganglia, in which paralysis agitans, pseudosclerosis, Wilson's disease, double athetosis and chronic progressive chorea are included. The still indeterminate pathology of these conditions is carefully and on the whole fairly reviewed. The other chapters that have undergone most modification are those on the diseases of the fore-brain, in which epidemic encephalitis is now included; that on the neuroses, in which the recent work on the nature and origin of hysteria receives adequate attention, and that on the angio- and tropho-neuroses.

The type and the reproduction of the illustrations are excellent, the editing seems to be extremely efficient, and the very complete index at the end of the volume increases its value as a book of reference, and makes it almost indispensable to all workers in clinical neurology.

Miners' Nystagmus. First and Second Reports of the Medical Research Council Committee. London: H.M. Stationery Office. 1922 and 1923.

These reports include a summary of the primary conclusions of the Committee, a general report on miners' nystagmus, a report on the psychoneurotic symptoms associated with it, and sections on the incapacity resulting from the affection, and on the importance of errors of refraction in its pathogenesis.

The chief conclusion to which the Committee has come is that deficient illumination, due to the low illuminating power of the safety lamps and the great absorption of light by the coal, is the essential factor in the production of miners' nystagmus, They regard all other reputed factors as of little or no importance; they fail, for instance, to find any evidence that errors of refrac-

tion have an influence upon the disease. Their conclusions that the common belief among miners that there may be permanent damage to vision, or even total loss of sight if underground work is continued, is baseless, is obviously of great economic as well as of medical importance.

The section on the psychoneurotic symptoms of the disease suffers from the obvious lack of personal experience of the writer with the conditions he discusses and attempts to analyse.

Le Cerveau et la Pensée. Par HENRI PIÉRON. Pp. iv, 328. Paris: Félix Alcan. 1923. Price 10 fr.

More than one volume with a similar title and a more or less identical object to the book under review has appeared in the past, but to-day when our knowledge of the structure and functions of the nervous system is increasing rapidly, and in a period when psychology has become more objective and biological in its methods and has consequently thrown new light on the mode of working of the mind, the considered views of the Director of the Laboratory of Physiological Psychology at the Sorbonne cannot fail to be of interest.

This book, which belongs to "La Nouvelle Collection Scientifique," has been written for the layman rather than the specialist, but even the latter will find in it much of interest and instruction. The main thesis of the author is that before we attempt to interpret the functions of the brain in their relation to the functions of the mind, it is essential to understand the main principles at least of the physiology of the elementary nervous mechanisms; and that it is only when psychology approaches its problems from the point of view of the biological sciences, and especially of physiology, that it can attempt to solve or understand the nature of the mind.

Diagnostic et Traitement des Sciatiques. Par H. ROGER et G. AYÈMS. Pp. 164, avec 15 figures. Paris: Maloine et Fils. 1923. Price 8 fr.

This small book deals concisely but clearly with one of the commonest of nervous affections. The most interesting and valuable chapters are those in which the clinical features of true sciatica are contrasted with those of the "false sciaticas" where the pain does not arise from an affection of the nerve itself; with the symptomatic sciaticas, the term which the authors apply to painful affections of infective or toxic origin; and with the pains of sciatic distribution due to compression or other gross disease of the sensory roots or of the nerve.

A large part of the book is devoted to the treatment of the different forms of sciatica, and in this section even the most experienced clinician may find valuable hints.

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EDITOR.